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# A TEXT-BOOK OF SURGICAL PATHOLOGY

By

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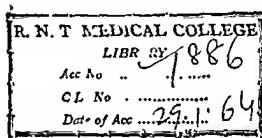
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## PREFACE TO THE SIXTH EDITION

THE need for a new edition has made it possible to carry out a general revision and to make a number of alterations

Some sections, for example, those dealing with thrombo phlebitis, brachial neuritis, sciatica, peptic ulcer, splenic anaemia, and intestinal obstruction have been rewritten

There have been added, *inter alia*, descriptions of vascular hypertension, cruralgia, and tumours of muscles. There is, too, a new chapter on diseases of the pericardium, the heart, and great vessels

Some of the older illustrations have been replaced by clearer examples, and a number of new ones have been brought in. The size of the book is unaltered.

The book is intended for senior students of surgery, for whom it is hoped it will continue to be of value

Our thanks are due to the publishers for their care and courtesy in the preparation of the new edition

C F W ILLINGWORTH

B M DICK

GLASGOW

## PREFACE TO THE FIRST EDITION

THIS book has been written for graduates and senior students with the object of providing an account of the pathology of surgical diseases, and especially of those aspects that are outside the scope of text books of general pathology.

We have emphasized those features that are of greatest value to the surgeon, and we have laid particular stress upon conditions that are brought to view in the operating theatre and the surgical laboratory, but we have included also such relevant information as can be gained in the pathological department, in the post mortem room or in research laboratories.

Presuming a certain knowledge of general pathology on the part of our readers we have made only passing reference to such fundamental processes as inflammation, suppuration, ulceration and repair. Their omission has given us room to expand certain subjects in directions which, we hope, will increase the readers' interest. For example in the chapter on Tumours we have referred at some length to experimental researches, and to modern views on the precancerous state and on the nature of tumour formation, in the chapter on Diseases of Bones we have discussed various theories of the growth, modelling and repair of bone, and in the chapter on Diseases of the Thorax we have included much that is usually dealt with only in special works.

The labour of preparation has been lightened by the encouragement which our many colleagues have combined with their advice and assistance. Our especial gratitude is due to Mr D M Greig, Conservator of the Royal College of Surgeons of Edinburgh, who has offered many stimulating suggestions and helpful criticisms and has corrected the greater part of the script. Our thanks are due also to Professor D P D Wilkie and to Mr J M Graham, who have given much helpful encouragement, to Dr E B Jamieson, who has read a considerable portion of the book, and criticised it constructively, and to Mr J J M Shaw and Dr Douglas Miller, who have given valuable advice in regard to the chapters on Tumours, and Diseases of the Female Generative Organs respectively.

In the matters of illustrations our colleagues have been equally helpful. Mr Greig has permitted us to use many specimens from the College museum and has lent many photographs from his own collection. Professor Wilkie has allowed us the full use of the University Department of Surgery, and Professor J Fraser and Professor R W Johnstone have provided similar facilities in the Departments of Clinical Surgery and Diseases of Women, respectively. We are grateful to Mr J W Struthers for the loan of several valuable specimens from his collection. These illustrations and those lent to us by other friends are acknowledged individually in the text.

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Almost all the photomicrographs are from the cabinet gallery of the Royal College of Physicians of Edinburgh, and are the work of Colonel W. F. Harvey, I M S, and Mr. T. D. Hamilton. To them, and to the laboratory committee, we would express our great indebtedness.

We are indebted to Miss McLarty for many of the drawings, to the technical staff of the University Department of Surgery for some of the photographs, and to Miss M. Robertson for her care in preparing much of the typescript. Lastly, we have to thank Mrs. C. F. W. Illingworth, who has typewritten a large part of the manuscript, and whose constant encouragement has done much to lighten the task of preparation.

C. F. W. ILLINGWORTH

B. M. DICK.

EDINBURGH,  
*December, 1931*

# SURGICAL PATHOLOGY

## CHAPTER I

### INFLAMMATION

INJURY or infection insufficient at once to impair the vitality of tissues stimulates the reactive process known as inflammation. Since the effects of injuries and infections constitute a large part of a surgeon's work, the study of inflammation may justly be regarded as of fundamental importance to the surgeon pathologist.

Inflammation may be caused by a number of physical and chemical agencies, including physical trauma, irritation by foreign bodies, heat, cold, light, electricity, X rays and radium. Inflammation may also be caused by pathogenic bacteria, and this is by far the most important type. Inflammation may be acute or chronic, according to the intensity and duration of action of the causative agent, and various degrees of both acute and chronic inflammation occur, according to the specific type of bacterium or trauma responsible.

The inflammatory reaction occurs as a response to the irritant effects of toxins secreted by the bacteria; or, in the case of aseptic inflammation, of the products of tissue breakdown at the site of injury. Generally, the changes in acute inflammation are concerned mainly with neutralizing, destroying and eliminating the causative agents, and they involve varying degrees of damage to the affected part. In chronic inflammation, on the other hand, whilst destructive changes are still apparent they are of a lesser degree, and are often merged in or obscured by changes of a reparative nature—the process of repair.

Acute inflammation, in its broadest sense, includes three distinct processes—the local vascular phenomena at the site of the lesion, the local reaction of the fixed tissue cells, and the constitutional effect characterized by leucocytosis and antibody formation.

The local vascular phenomena are responsible for the classical features of acute inflammation. The blood vessels become dilated and render the part red and hot, blood plasma exudes from the dilated vessels and causes swelling, the sensory nerves, irritated by toxic substances and perhaps compressed by oedema, give rise to pain, and finally muscles, joints and glands within the inflamed area suffer in varying degree impairment of function. Thus originate the five cardinal signs of inflammation—*rubor*, *calor*, *tumor*, *dolor* and *functio læsa*.

The first exact description of the vascular changes in acute inflammation we owe to Cohnheim, and it is no exaggeration to claim that his observations, as recorded in his *Lectures on General Pathology* in 1877, form the beginning of our conception of inflammation.

Cohnheim's studies were mainly carried out upon the frog, and the most instructive are those in which he examined the microscopic changes in the vessels of the mesentery, in which inflammatory changes were induced by the application of weak acids.

The earliest change observed at a site of inflammation affects the smaller blood vessels, especially the smaller veins and capillaries. After an inconstant and transient constriction these vessels become dilated, sometimes to twice their ordinary size. Not only do the vessels dilate, but also innumerable capillaries which in the normal tissues have been empty, collapsed and unrecognizable, now become visibly distended. The immediate result is a greatly accelerated blood flow through the affected part, but after a short time—rarely more than half an hour—a further change becomes apparent. Although the total blood flow through the part remains greatly increased—witness the local heat—the flow through the individual vessels becomes reduced. Indeed, in severe cases the stasis is so marked that the individual blood cells can be recognized not only in the capillaries, but also in the veins and even during diastole, in the smaller arterioles.

It seems probable that this slowing of the blood stream is attributable to two factors. The first is that the endothelial cells lining the vessels, normally of flattened character, at this stage are affected by the bacterial or other toxins and become swollen, so that they project into the lumen of the vessel and partly obstruct it. The second factor is that as a result of the escape of its fluid content into the tissues the blood now becomes more viscous and flows less freely.

Now appears one of the most striking phenomena in the whole process. In Cohnheim's words, "the eye of the observer hardly has time to catch all the details of the picture before it is fettered by a very unexpected occurrence." Usually this takes place in a vein, less often in a capillary, and it consists in the emigration of the leucocytes through the vessel wall into the tissue spaces.

Normally, in the veins the blood cells tend to occupy the central or axial part of the stream, whilst the peripheral or plasmatic zone consists mainly of plasma with an occasional leucocyte. In inflammation, as the blood flow becomes sluggish, this disposition is lost, and the original plasmatic zone fills with innumerable leucocytes, which move slowly and unevenly, as though driven along by the blood flow and yet held by a cohesive property of the endothelium. Eventually the internal surface of the vein appears paved with an unbroken layer of leucocytes. Now begins the leucocytic emigration proper—it almost looks as though the leucocytes squeeze themselves through the vessel wall between intact endothelial cells, and gradually resume their original shape on reaching the perivascular tissue spaces. The minute gaps left after their passage appear to be sealed immediately.

The migration of the leucocytes does not cease when they have left the vessels. Partly carried by the flow of plasma, partly attracted by chemotaxis they are drawn towards the seat of inflammation. There they secrete enzymes with bacteriolytic properties, they engulf organisms or minute foreign bodies, or they may themselves be destroyed by the bacterial or other toxins.

In the wake of the leucocytes, red blood cells also may escape from the vessels by the process of *diapedesis*. This is not a striking feature in the majority of inflammations, but occasionally it is conspicuous.

Keeping pace with the cellular migration, there occurs a transudation of plasma into the tissue spaces or on to the serous surfaces. This transudation is due partly to the toxic damage to the capillary and venous walls, which impairs the permeability of the endothelial membrane. It is also attributed to the fact that the tissue colloids, which are of low osmotic pressure, and are broken down by the bacterial or other toxins into crystalloid substances, which, being of relatively simple composition, exert a high osmotic pressure and consequently withdraw fluid from the vessels.

Escape of blood plasma is a potent factor in the defence against bacterial infections, for it not only dilutes the toxins but also exposes them to antibodies and supplies opsonins which facilitate phagocytosis.

In some circumstances, especially when poured out upon a serous surface, the fibrinogen rich exudate becomes clotted, and this may have additional value as a means of circumscribing an infection. This is seen most strikingly when an acute appendicular infection is circumscribed by fibrinous adhesions between the surrounding coils of intestine.

**The Nature of the Leucocyte Response.** One of the most remarkable features in the whole process of inflammation is the behaviour of the leucocytes, particularly, in acute infections, of the polymorphonuclear leucocyte.

Reference has already been made to the emigration of the leucocyte—how it settles to the periphery of the blood stream, ranges itself alongside the vessel wall, extrudes itself between the endothelial cells, and finally moves in the tissue spaces towards the focus of inflammation. Recently a tissue product—‘leucotoxine’—has been isolated in crystalline form from injured or inflamed organs, which, when applied locally in minute dilution has an exceedingly powerful effect in accelerating capillary permeability and accumulation of leucocytes.

Leucocytes within range of any particulate matter—a minute foreign body or a bacterium—may exhibit the phenomenon of phagocytosis (*phagēin*—to eat). First the cytoplasm on the side nearest the particle bulges, and then projections or pseudopodia appear, which encircle the particle and draw it into the substance of the phagocyte. Within the cell the particle is subjected to the action of enzymes and digested or dissolved—or, this failing it may be discharged from the leucocyte and set free again in the tissue fluid.

It is interesting to note that the property of phagocytosis, so beautifully seen *in vivo*, is entirely lost in *in vitro* experiments if the leucocytes are first washed in physiological saline. From this it is clear that some elements from the body fluids are required to facilitate phagocytosis. These accessories are known as opsonins (*ôpsôn*—a sauce). They are present in normal blood plasma, and are found in greatly increased amount in the plasma of patients whose immunity is raised in response to an infection.

The phenomenon of phagocytosis by leucocytes was discovered by Metchnikoff almost by chance in the course of a general inquiry into

the cellular responses to injury shown by the simpler forms of life. A rose thorn embedded in the larva of the starfish was found to elicit a cellular response to all intents and purposes the same as in animals possessing a vascular system. From these observations Metchnikoff concluded that phagocytosis is not merely an important feature, but the essence of the defence against injury or infection, in other words, all the other phenomena of inflammation merely form the mechanism evolved by the higher forms of life to bring the leucocytes more rapidly to the field of action. This simple view is not, however, to be accepted. Whilst the leucocytic response is of undoubted importance, there are many other factors involved in the defence against infection.

The mechanism of leucocytic emigration and phagocytosis is one of great biological significance, and it is now generally agreed that these processes can best be explained by applying the known laws of chemistry and physics. They really depend upon the inter-related properties of chemotaxis and amoeboid movement.

The term *chemotaxis* was suggested by Pfeffer in 1881 to describe a phenomenon exhibited by the spermatozooids of certain ferns which were powerfully attracted by dilute solutions of maleic acid, a substance contained in the female sperm cell of the fern. A similar property was demonstrated by Stahl in his classical experiments with a jelly-like plasmodium growing on the bark of trees. Stahl showed that *in vitro* the plasmodium is attracted towards a drop of infusion of oak bark, provided it is in sufficiently dilute solution. Moreover, he noted that the plasmodium moves towards the drop by a process of protoplasmic streaming closely similar to amoeboid movement.

The chemotactic effect of a substance towards leucocytes may be tested by placing the substance in the open end of a capillary tube and inserting the tube within the peritoneal cavity of an animal, when positive chemotaxis is indicated by the aggregation of leucocytes round its open end. Many substances have a positive chemotactic action, whilst others are neutral, and others again are said to have a negative action *i.e.* repel the leucocytes.

Chemotaxis is now recognized to be a surface tension effect (see below). If the solution has the effect of reducing the surface tension of the leucocyte on the side nearest to it, the leucocyte travels in that direction. The property of phagocytosis also is now regarded as a comparatively simple physical process resulting from changes in surface tension. Phagocytosis is not, of course, peculiar to the leucocyte, but is enjoyed by all unicellular organisms and is one of the most striking characteristics of the amoeba. An amoeba may be looked upon as a drop of a colloidal solution enclosed in a delicate semi-permeable membrane, and its movements are related to changes in surface tension which, in turn, depend upon changes in the character of the cellular protoplasm or of the fluid in which it is immersed.

Both chemotaxis and amoeboid movement may be imitated by "artificial amoebæ" composed entirely of non-living substances. Thus a drop of clove oil suspended in a mixture of glycerol and alcohol performs movements almost identical with those of the amoeba—it responds to chemotaxis and exhibits "phagocytosis."



Chemotaxis may be demonstrated if a small quantity of stronger alcohol is injected into the fluid near to the drop of clove oil. The alcohol reduces the surface tension on the one side of the drop, the drop thereupon bulges on that side and moves in the direction of the stronger solution. Phagocytosis is best imitated by an "artificial amœba" consisting of a drop of chloroform suspended in water. When such an amœba comes within range of a minute particle of shellac or paraffin or balsam, it sends out pseudopodia, engulfs the particle and then digests (*i.e.*, dissolves) it. If the particle is in the form of a thread, it may be engulfed even though it is several times longer than the diameter of the drop, being gradually drawn in and coiled up inside until completely ingested. Other types of particle, on the other hand, the chloroform amœba will reject, for example, fragments of glass or wood. The most remarkable behaviour of all is witnessed when a fragment of glass coated with shellac is offered to the "chloroform amœba," for this compound particle is readily ingested, but when the shellac has been dissolved within the drop the glass is extruded.

**Suppuration** Suppuration results when there is a nice balance between the infecting agent on the one hand and the inflammatory reaction on the other. The combined effects of the leucocytes and the antibodies contained in the inflammatory exudate have circumscribed the infection, yet failed to destroy the causative organisms. Many of the phagocytes are themselves destroyed by the bacterial toxins, and they and their enzymes and liquefaction products are the main constituents of the pus. In severe spreading infections the appearance of pus indicates that the infection has been circumscribed. Under these circumstances "laudable pus" is indeed welcome.

Pus formation is due essentially to the progressive emigration of leucocytes in large numbers, and it depends upon the continued production of chemotactic substances by the infecting agent. The pyogenic cocci are the commonest causes of suppuration, whilst coliform bacilli and many other organisms may be responsible, though less frequently. Aseptic irritants, *e.g.*, foreign bodies, are less common causes of suppuration.

The leucocytes present in pus secrete proteolytic enzymes, and as many of the leucocytes are killed by the bacterial toxins and undergo disintegration their intracellular enzymes are also liberated. The digestive action of pus is manifest by its effect in loosening adherent sloughs in such conditions as cellulitis. In any suppuration, indeed in any severe inflammation, there is inevitably some destruction of the specialized tissue cells, sometimes amounting to massive necrosis of the part. It is the function of the enzymes of pus to digest and liquefy such necrotic tissues, so that they may be reabsorbed or, failing this, discharged when the abscess is fully established.

This consideration should be kept in mind in the surgical treatment of suppuration. If pus is present the natural reaction of a surgeon is to let it out, to terminate the toxæmia caused by septic absorption from the abscess. It must be remembered, however, that the enzyme effects of pus are often beneficial, and if the toxæmia from absorption is not too severe a more conservative attitude is often advisable, particularly in

conditions characterized by extensive necrosis of tissues. This has been the accepted practice in the treatment of boils, carbuncles, acute mastitis and similar infections, delaying incision until the sloughs have been liquefied by enzyme action.

**Types of Inflammatory Cells** In the foregoing account of acute inflammation and suppuration the cell of most conspicuous importance has been the polymorphonuclear leucocyte. This is the cell evoked by all the common causes of acute inflammation, and may be regarded as the first line of defence against acute infections. In the later stages of acute inflammation, and in chronic inflammation, other cells appear and occupy more important positions in the tissue reaction.

The large mononuclear cell or macrophage takes an important part in clearing up or scavenging after the acute phase of inflammation is past. This cell, variously known as a polyblast, a clasmatocyte, or an adventitial cell, is a large, pale, rounded cell with a vesicular nucleus and abundant cytoplasm. It is believed to be derived from the histiocytes or wandering cells of the tissues, from the cells of the reticulo-endothelial system, or possibly from the large mononuclear cells of the blood. Its main function is to scavenge by phagocytosis the debris left by the acute inflammatory reaction, and thus it may engulf red cells, dead polymorphs, blood pigment, foreign particles and fragments of dead tissue. In some cases, where there are larger fragments of foreign material to be removed, several macrophages fuse, forming giant cells allied to the foreign body giant cells.

Lymphocytes are rarely seen in acute inflammations, except in the central nervous system, where they are regularly present in such conditions as poliomyelitis and meningitis. They are more characteristically present, however, in chronic infections and in specific conditions such as tuberculosis, syphilis and actinomycosis. Lymphocytes have little or no phagocytic activity, and migrate much more slowly than polymorphs in response to chemotaxis.

Plasma cells are also characteristic cells of chronic inflammatory conditions. They are mononuclear cells, somewhat larger than lymphocytes, with an eccentric nucleus and a basophil cytoplasm which contains in its centre a clear area close to the nucleus. Plasma cells and lymphocytes together constitute the "small round cells" of chronic inflammatory exudates.

Eosinophil cells are normally present in the blood in small numbers (2 to 4 per cent) and are occasionally found in inflammatory infiltrations. They are most characteristically present in allergic conditions and in parasitic infestations, and it seems likely they may appear in response to the irritation of foreign proteins.

### Repair

Following rapidly upon inflammation and indeed merging with its later phases, comes the process of repair. This process varies in character according to the particular type of tissue involved in the inflammatory reaction and the degree of destruction. In general, the greatest capacity for regeneration is shown by areolar and fibrous

tissues and by covering layers of epithelium, whereas the secreting cells of glands, the cells of the central nervous system and muscle cells undergo regeneration to only a small extent. In these latter tissues the process of repair consists mainly in filling the defect by fibrous tissue. Thus a wound of muscle is followed by very little proliferation of muscle cells, and the defect is repaired by a growth of scar tissue.

The process of healing may be seen in its simplest form in a clean incised wound of the skin. Microscopically, the first evidence of healing may be seen within 24 hours, both in the connective tissues and the epidermis.

In the connective tissues young capillary vessels bud out from existing vessels at the margin of the wound and invade the blood clot occupying the wound. Around the capillaries appear fibroblasts, and

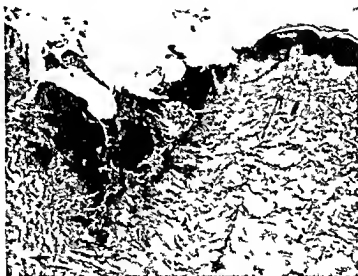


FIG. 1. Wound of integuments twenty four hours old. The cavity of the wound (on left) is filled with clot. Early inflammatory changes are seen at the margin.

with them come large phagocytic cells, scavengers of any dead material. The fibroblasts proliferate actively and form a young connective tissue known as *granulation tissue*. Later the fibroblasts give rise to the formation of collagen fibrils, whilst the cells themselves become reduced in size and cease to proliferate, so that eventually the granulation tissue is converted into fibrous tissue of adult type.

Simultaneously with these changes in the connective tissues healing proceeds in the epidermis. At a very early stage epidermal cells extend from the wound margin into or over the surface of the blood clot. To some extent this process is due to multiplication of the marginal cells, but much of it is due to sliding of the adjacent epidermis in towards the wound. This is seen well in wounds of the rabbit's cornea. In this animal, pigment in the basal cells of the limbal epithelium forms a complete brown ring round the limbus, after a wound of the cornea sliding of the epithelium is demonstrated by centripetal displacement

of that part of the ring close to the wound. At first the new epidermis is thin and unkeratinized. Later it approximates to normal epidermis, but lacks sebaceous or sweat glands and hair follicles.

In large wounds healing is delayed by the simple difficulty of filling the defect. The same inflammatory reaction occurs, and the cavity of the wound is filled by a coagulum of blood and lymph containing many leucocytes. Capillary loops and fibroblasts grow into the coagulum from the surrounding tissues and sooner or later line the wound with granulation tissue which later becomes fibrous. Contraction of the



FIG. 9. Wound of the integuments three days old. The cavity of the wound (left) is filled with clot. There is a vigorous downgrowth of epidermis over the edge of the wound.

young fibrous tissue then occurs and this has a valuable effect in reducing the size of the wound.

Whilst these changes are occurring in the depths of the wound the epithelium round the margin proliferates and grows over the defect as a thin blue layer, easily damaged by moving the part or by tearing off adherent dressings. In the case of large wounds the epithelial growth may prove insufficient to cover the whole defect especially if a chronic infection persists or if the part is of poor vascularity, for owing to lack of adequate nutrition from the underlying connective tissues the epithelial ingrowth becomes progressively slower and the centre of the wound is left open as an ulcer. In such cases the epithelium covering the wound margins is thin, blue and adherent and is very easily devitalised.

Shrinkage of the tissues plays an important part in healing, part,

cularly in large wounds. It is an everyday experience that the eventual scar is always much smaller than the original wound, and in some cases the area of the raw surface is reduced by 75% as a result of this process.

**Factors influencing the Rate of Wound Healing** The rate of wound healing is affected by many factors both local and constitutional.

(1) *Vascularity* Wounds of the face heal with great rapidity (despite constant movement) and so do wounds of the scalp whereas wounds of the less vascular skin of the trunk and limbs are much slower. If the blood supply to a part is seriously diminished, as a result, for example, of local scarring or obliterative vascular disease, healing may be greatly delayed.

(2) *Lymph drainage* Impairment of lymph drainage slows up the



FIG 3 Wound of integuments ten days old. The wound is filled with young connective tissue and completely covered by epidermis. Some islands of epidermal cells are included in the scar.

process of repair, as is seen clearly in the healing of a part oedematous from any cause. The beneficial effect of elevation of a wounded limb is due to the improvement which results in lymphatic drainage, while the effect of firm pressure, such as is produced by encasing the part in plaster, is attributable to the same cause.

(3) *Movement* Movement of the wounded part is well known to delay healing and indeed immobilization is a cardinal principle of treatment. Immobilization not only prevents damage to the young granulation tissue and covering epithelium, but also diminishes greatly the flow of lymph through the affected part and this factor also appears to have a beneficial influence. Apart from delay in healing movement also leads to the formation of large unsightly scars, witness the 'keloid' cicatrix of many wounds of the neck as compared with the thin linear and almost invisible scar in a limb immobilized in plaster.

(4) *Anchorage to subjacent tissue* Reference has already been

made to the part played by shrinkage of the wound. If the margin or base of the wound is anchored to a subjacent bone or ligament or fascia—the result, for example, of infection—shrinkage cannot occur and healing is delayed. This is well seen in the chronicity of varicose ulcer, of deep wounds involving bone, and of the incision in cases of osteomyelitis.

(5) *Foreign bodies and irritant applications*. Apart from inert materials such as stainless steel and vitallium, nearly all foreign bodies induce a reaction which impairs the process of healing. The reaction varies from a minimum connective tissue response to all grades of inflammation according to the irritant character of the substance and the degree of infection associated. In the more severe types the



FIG. 4. Wound of integuments thirteen days old. High power view showing character of the young fibrous tissue occupying the wound. The epidermis is undergoing keratinization.

whole process of healing is held up until the foreign body has been extruded.

Necrosis at the wound margin, whether due to impaired vascularity or to infection, has the same effect. Here healing is delayed until the dead tissue has been loosened by phagocytic action and cast off as a slough.

Antiseptics applied to a wound may have a similar effect inasmuch as they are harmful to the living cells. Indeed, some antiseptics are more effective in delaying the process of healing than the infection they are designed to prevent.

(6) *Infection*. Of all the local factors which influence wound healing infection is undoubtedly of the greatest practical importance. Toxins of bacterial origin destroy the marginal epithelium and connective tissue cells, and the presence of fluid and cellular inflammatory exudate also delays the healing process, while in some cases the formation of sloughs is a further factor. Much depends upon the nature of the

infecting organism and it is generally agreed that a streptococcal infection is most harmful. The physical state of the infected wound is of even greater importance. Thus a completely open surface wound may heal at almost the normal rate despite heavy infection, while a deep wound, especially if closed by sutures, by creating conditions of tension under which necrosis occurs, may heal only after much delay.

(7) *Constitutional factors* Wound healing is generally delayed in diabetes and severe anæmias. Hypoproteinaemia is an important factor. Following all types of injury there is a considerable loss of nitrogenous substances in the urine as a result of protein catabolism, the cause of which is obscure. Moreover in an infected wound there may be a local protein loss in the exudate. At the same time the protein intake may be low by reason of anorexia. In the healing wound moreover, there is an increased demand for protein for the growing cells and new tissues. The effect of lack of protein is to cause oedema and to impair the formation of fibroblasts. Deficiency of vitamin C has recently been shown to be important and may be the factor responsible for the delayed healing of operation wounds in patients suffering from gastro intestinal diseases such as carcinoma of the stomach and peptic ulcer in whom the absorption of vitamin C has been defective. The frequency of 'burst abdomen' in such cases has been attributed to this factor. It has been shown that the part played by vitamin C is to facilitate the restoration of collagen. In deficiency states the early phases of wound healing proceed normally, but collagen fails to develop, the wound does not consolidate and tends to stretch or give way at a later stage.

*Wound stimulating Substances* Since prehistoric times men have searched for substances capable of accelerating the healing of wounds. In recent years particular attention has been directed to embryonic extracts, some of which are known to accelerate the growth of cells in tissue culture, to various substances affecting surface tension, and to particular agents such as allantoin, red cell suspensions and chemicals with the sulphhydryl group (SH). At the present time none of these substances has been shown to be of practical value. Indeed, when one observes the headlong rate of healing as seen microscopically in a simple clean untreated wound, it becomes obvious that no method of hastening this process is likely to be more effective than that of putting the wound at rest and countering the influences adverse to healing.

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## CHAPTER II

### WOUND INFECTIONS

THERE are no boundaries in scientific endeavour, and our knowledge of wound infections is the outcome of the labours of the pioneers of Listerian and aseptic principles and steady advances in bacteriology, immunology and therapeutic practices, the greatest of which is the discovery of antibiotic agents

Nowadays in hospital wards we seldom witness the once common ravages of erysipelas moist gangrene and uncontrolled case-to-case infection. Though we may feel more secure wound infections on a lesser scale are still common and are a continued source of difficulty and anxiety in all fields of surgical work so that study of the basic factors governing their origin propagation and control is of the highest importance. Indeed it is a first principle of surgical teaching.

Wound infection is the result of implantation of pathogenic bacteria upon or within a breach of the cutaneous serous or mucous surfaces of the body. The portal of entry may be an obvious wound or the most insignificant abrasion, scratch or prick. In either case the ensuing infection may lead to severe damage to the part primarily infected, to grave constitutional disturbance and to lesions in distant organs, any one of which may exceed the original infection in importance and severity.

**Predisposing Factors** Susceptibility to wound infection may be conditioned by constitutional or local factors. Frequently these are combined.

(1) In some persons even though seemingly robust, there is an undeniable lack of resistance to certain types of infection the underlying cause of which is not understood. Sometimes the susceptibility is familial, more often it is an individual peculiarity. Constitutional susceptibility may also be caused by debility resulting from acute or chronic illnesses, diet deficiency diabetes etc. which favour the occurrence and propagation of infection. The diminished immunity may be accounted for by impaired local tissue activity and by reduction in the bactericidal properties of the blood.

(2) The local factors which influence infection are largely governed by the quality of the leucocyte response. Consequently, parts which are highly vascular are relatively immune from severe infections and are more able to circumscribe them promptly and vigorously as compared with tissues of less vascularity. Thus wounds of the face seldom become infected, whereas in wounds of avascular structures such as tendons or cartilage, the tissues show poor defence and often undergo necrosis.

The special characteristics of the wound may have an important



bearing upon the severity and course of an infection. Contusions and lacerations provide a favourable foothold for bacterial growth, especially if there is contamination with extraneous matter, and the resulting infection is often severe and attended by sloughing and considerable toxic absorption. Punctured wounds, such as may be sustained in conducting a post-mortem examination, may be equally dangerous, because infective material (sometimes with foreign matter) may be implanted at considerable depth and the narrow outlet prevents the escape of inflammatory products.

The skin and subcutaneous tissues are more resistant to infection than the serous membranes of the body. For example, a trivial infection of a joint, such as the knee, is often followed by severe and extensive inflammatory change.

Sometimes a part already infected, e.g., a chronic ulcer, affords access for more virulent organisms, and the existing reactive processes may limit the severity of the infection. Superadded infection of more recent wounds is common, and sometimes of serious consequence.

### Bacteriology of Wound Infections

The most important bacteria in the causation of wound infections are the pyogenic streptococci and staphylococci. In special circumstances there may be a concomitant or superimposed infection by other organisms such as *B. coli*, *B. pyocyaneus*, pneumococci, *Cl. tetani* and *Cl. welchii*.

**The Pyogenic Streptococci.** The streptococcus group is very heterogeneous and complicated classifications of various groups, types and strains have been formulated. For practical purposes, however, regard need be taken only of two chief types, the hæmolytic and the non hæmolytic.

The hæmolytic streptococci are frequently found in the nasopharynx, and streptococcal infections may originate from this site or from external sources. They are apt to cause acute spreading infections such as erysipelas, cellulitis, lymphangitis, etc. They are of especial importance as the commonest cause of puerperal sepsis (p. 679).

As the manifestations of the diseases produced by the hæmolytic streptococci are so varied many attempts have been made to formulate a cultural or biological standard to account for the differences. Lancefield and others, approaching the problem from a serological standpoint, classify hæmolytic streptococci into groups according to their agglutination reactions. Most of the hæmolytic streptococci isolated from infections in human subjects belong to group A. Streptococci of other groups designated (B C D E and H to K), which have been obtained from a variety of human and animal sources, are, with few exceptions, non pathogenic for man. Nowadays it is of greater importance to ascertain the degree to which the organism is sensitive to penicillin.

The non hæmolytic streptococci (which lack diffusible toxins) have a much lower virulence. They are normally found in the mouth (e.g., *str. viridans*) and the bowel (*enterococcus*). They are responsible for many low-grade infective processes, e.g., dental sepsis, peptic ulceration, cholecystitis. They are common commensals in mixed

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infections In rare instances anaerobic types of streptococci are encountered They are usually non hemolytic and of low virulence

Pathogenic streptococci elaborate a diffusible toxin which varies in amount and character in different strains The toxin contains a leucocidin and a fibrinolytic agent, and it is probable that the virulence of different strains is governed by the extent of production of these substances

**Staphylococci.** The staphylococcus group includes the commonest commensals and pathogens in man These organisms occur in the throat, on the skin, in hair follicles and in sebaceous glands There are two fairly distinct types, the highly pigmented *Staph aureus* and the paler *Staph albus* Of these, the former is the more pathogenic in man and gives rise to pustules, boils, whitlows and carbuncles, and also to the great majority of cases of acute osteomyelitis

The pathogenic power of staphylococci is due almost entirely to the exotoxins they produce These contain (1) an  $\alpha$  lysin, which gives rise to skin necrosis in addition to other toxic effects, (2) a  $\beta$  lysin, of uncertain action, (3) a leucocidin, and (4) coagulase, which is responsible for the clotting of plasma The toxins of staphylococci evoke a vigorous antitoxic response in the blood Like other exotoxins they can be changed to toxoid by the use of formaldehyde, and in such attenuated form have been used for immunization

**Bacillus coli** The *Bacillus coli* occurs naturally as a commensal in the intestinal tract It is a common cause, either alone or with other organisms of inflammatory and suppurative lesions within the abdomen, e.g., peritonitis cholecystitis appendicitis In such diseases the pus has a characteristic faecal odour *B coli* is also often responsible for inflammatory lesions in the urinary tract, e.g., pyelitis and cystitis In general the organisms cultivated from such lesions are more virulent than the ordinary intestinal strains

**Bacillus pyocyaneus** This organism which occurs naturally in decomposing organic matter, sometimes gives rise to a stubborn form of superimposed infection in wounds It rarely occurs alone In wounds it gives rise to a characteristic green or bluish coloration of the pus owing to the production of a pigment pyocyanin

### Source of Wound Infections

A wound may be infected by organisms already present in the skin or mucous membranes or by organisms introduced from without

The skin is a common source of wound sepsis, for it frequently harbours pathogenic organisms, especially staphylococci and streptococci

Skin organisms vary greatly in number and virulence Some persons harbour staphylococci of high virulence in large numbers, others have relatively few pathogens This disparity is related to certain occupations, thus doctors, nurses and others handling septic material may harbour dangerous organisms, and so to a smaller extent may butchers and fishmongers, whereas at the other extreme in motor mechanics and engineers working with oil and metal filings the skin of the exposed parts is commonly almost sterile

Organisms introduced from without include the common pyogenic cocci and also the streptococcus of erysipelas, the bacillus of tetanus, and the anaerobic organisms of gas gangrene

Contamination of operation wounds is a subject of greatest concern to the operating surgeon, and one which places a great responsibility upon those who supervise the aseptic ritual at operations. Apart from its immediate effect in causing wound suppuration, such contamination may play a part in the etiology of phlebitis and pulmonary embolism, and is doubtless of importance also in causing adhesions and leading to keloids and painful scars

The incidence of wound infections bears a close relationship to the duration of exposure of a wound to the air. Thus in lengthy operations, e.g., on the brain, a careful technique is of especial importance

The commonest type of post operative wound infection is the "stitch abscess," which usually develops ten days or two weeks after operation, giving rise to a small suppurative collection of low grade virulence in the skin and subcutaneous tissue. The infecting organism is generally the staphylococcus albus, and is doubtless derived from the adjoining skin, in which it commonly occurs as a commensal

More virulent infections of operation wounds are generally due to streptococci, and their invasion of the wound must usually be attributed to some breach of aseptic technique, although the possibility that the organisms may be endogenous, i.e., blood borne from some hidden focus of infection, cannot always be excluded with certainty

Staphylococci derived from the skin of the surgeon or his assistants may occasionally be responsible for infection of operation wounds. It must be realised that the most thorough "scrubbing up" cannot render the hands completely sterile, that organisms lying within the skin glands may be carried to the surface by perspiration during the course of the operation, and that such organisms may escape through minute glove punctures or through the sleeves of the surgeon's gown and thus contaminate the wound. In this connection it may be noted that unless particular care is taken, glove punctures occur in from 10% to 20% of operations. Fortunately, in most cases the organisms derived from a surgeon's hands are staphylococci of mild virulence, which readily succumb to the natural defence processes in the healing wound

One of the most important sources of infection of operation wounds is the throat of the surgeon or his assistants. Pathogenic streptococci hæmolytic and non hæmolytic, are commonly present in the pharynx in a large proportion of persons and their number and virulence are greatly increased in conditions of catarrh. The possibility of infection from this source (sometimes by 'carriers'), should be a reminder of the necessity for adequate safeguards against droplet infection in operation theatres

The importance of air borne infections during operation was well recognized by Lister, and it was to guard against this danger that he introduced the antiseptic spray. Later, as the incidence of the more virulent hospital infections diminished and the air of hospital wards and theatres became less subject to contamination, the need for air

sterilization became less obvious and the carbolic spray was abandoned. Recently, attention has again been turned to the risk of air borne sepsis, and such methods as ultra violet irradiation (Hart) or the use of fine antiseptic mists or aerosols (Pulvertaft) have been advocated

## SPECIAL TYPES OF WOUND INFECTION

### Erysipelas

This is a rapidly spreading non suppurative inflammation of the skin due to invasion by hemolytic streptococci. The streptococcus is not specific and does not differ in its morphological and cultural characteristics from other streptococci, *e.g.*, those responsible for puerperal sepsis. It does, however, usually run true to type, and may spread from case to case if strict precautions are not observed.

The organisms gain access through a wound or abrasion, often so small as to escape notice, and invade the lymphatics of the dermis. In the great majority of cases erysipelas affects the face or head. It generally originates near the mouth or nose, and may spread over the whole face and scalp, but does not usually invade the neck. Occasionally erysipelas affects the trunk, the scrotum, or the limbs gaining access at a wound or at such an infected surface as a chronic leg ulcer.

The affected skin is smooth, tense and fiery red. It is hot to the touch and tender on pressure. The spreading margin, which is irregular in outline, is clearly delimited and presents a raised edge. Minute vesicles are often visible, especially just behind the spreading edge, and the fluid they contain teems with streptococci.

The inflammation tends to be arrested in parts where the skin is tightly bound to underlying tissues. In parts where the skin is loose, such as the eyelids, much swelling develops as a result of oedema.

Microscopically the corium is oedematous and infiltrated with innumerable polymorphs and wandering cells, particularly those of mononuclear type. Streptococci abound in the tissues and the lymph channels.

Erysipelas (if untreated) continues to spread for from three to ten days and then terminates abruptly. If uncomplicated, it is generally not dangerous to life except in infants and in old or debilitated persons. Immunity following an attack is of short duration, recurrences of infection may lead to considerable obliteration of the lymph spaces by fibrosis resulting in a form of chronic oedema or elephantiasis.

### Cellulitis

This is an acute diffuse inflammatory process affecting the subcutaneous tissues and other lax connective tissue planes. It is characterized by extensive necrosis and sloughing of the tissues, with scanty pus formation as a later and secondary feature. The infecting organism is generally the *Streptococcus hemolyticus*, less often the *Staphylococcus*.

The infection may reach the subcutaneous tissues through a punctured wound or a comparatively small abrasion or prick, or from a neglected sore. The inflammation is often of sudden onset and spreads rapidly, and may be attended by severe toxæmia. The affected part

comes red, brawny and tense, whilst acute lymphangitis may be indicated by scarlet coloration and intense tenderness of the surrounding skin, and by red lines outlining the course of the main lymph vessels leading to the regional glands. As the cellulitis progresses, the skin comes transparent and shiny, and eventually becomes discoloured and separates, revealing grey necrotic sloughs beneath. In severe cases there may be massive necrosis amounting sometimes to gangrene of a part.

If the infection is of virulent type the regional lymph glands are involved early and may suppurate, or localized abscesses may develop at some point in the line of the lymph vessels. In severe cases septicæmia may supervene.

### Septicæmia and Pyæmia

These two conditions are closely related and may be grouped under the term Septicopyæmia. In septicæmia, organisms of the pyogenic group invade the blood stream and produce toxins which give rise to a characteristic illness. It is probably not true to say that the organisms grow and multiply in the blood stream. It seems more likely that the organisms establish themselves in the capillaries and sinusoids of the bone marrow, spleen and other tissues where they multiply and are liberated afresh into the blood.

In pyæmia, clumps of organisms or fragments of infected blood clot within the blood stream from a suppurative focus and give rise to metastatic abscesses.

Septicæmia must be distinguished from bacteræmia or bacillæmia. These latter terms are simply used to denote the presence of organisms in the blood. A bacteræmia may be transient and symptom free, a septicæmia is persistent and is associated with definite and often severe and continued intoxication.

**Septicæmia.** Septicæmia may originate from spread of the infection from an established suppurating focus or from a wound. Sometimes the origin is obscure and a pharyngeal or intestinal infection may be suspected, or puerperal or post-abortion sepsis.

Hæmolytic streptococci are responsible for over 50% of cases. The remainder are caused by staphylococci, pneumococci, and rarely *B. coli*, *pyocyaneus*, or the meningococcus.

**Streptococcal Septicæmia** is a common complication of puerperal sepsis, whilst another common cause is a punctured wound, often of trivial character, such as a pin prick. One of the most fulminating types of septicæmia is apt to follow a prick with an infected needle or instrument, sustained during a post-mortem examination. There are all too many cases on record in which such an apparently trifling accident has proved fatal within a few days.

The infection is characterized by severe toxæmia, with a high temperature, rapid pulse and raised respiratory rate. The parenchymatous organs of the viscera and the myocardium sustain cloudy swelling and fatty change, whilst in severe cases there are skin rashes and purpuric hemorrhages. Broncho-pneumonia and nephritis are common, especially in the terminal stages, whilst such complications as pleurisy,

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organism, but the danger of infected abrasions, whitlows, and punctured wounds should be more fully realised lest timely prophylactic measures are neglected. The spores are sometimes introduced with a foreign body such as a splinter of wood and may lie dormant until disturbed by a subsequent operation. Imperfectly prepared catgut has been responsible for tetanus after surgical operations. In exceptional cases no portal of infection is discoverable.

At the site of infection after an incubation period which may be as short as two, or as long as twenty one days a virulent toxin is liberated. The period may be prolonged to eight or more weeks if antitetanic serum has been given for prophylaxis. The toxin reaches the nervous system by the blood stream and along nerve trunks, and produces exaggerated reflex excitability within the motor cells, which is evidenced first by sustained spasticity in the related muscle groups and afterwards (if at all) by their spasmodic paroxysmal contraction. When the toxin reaches the nervous system it is at once fixed, and it cannot be detected in the cerebro spinal fluid. Its effect seems to be purely physiologic because at death there are no changes in the brain and cord, death is due to secondary effects such as cardiac and respiratory failure, hyperpyrexia, exhaustion, and pneumonia.

The route by which the toxin reaches the nervous system has been the subject of a prolonged controversy and has invited much experimental research. In man it seems to be absorbed mainly by the blood because its earliest effects such as trismus, difficulty in swallowing and rigidity of the neck muscles emanate from centres which could be involved only through the circulation. Transmission of toxin along axis cylinders of motor nerves, though it may occur in man, is more usual in animals, it leads to tonic contraction of muscles in proximity to the source of infection (*local tetanus*)\* which, as the toxin diffuses may become more widespread. In man the so called *cephalic tetanus* which may complicate severe head wounds, probably owes its rapid onset, accompanied by convulsions and paralysis of cranial nerves, to migration of toxin along nerve pathways.

The features and the severity of tetanus (if not modified by prophylactic serum) are, *inter alia*, conditioned by the amount of toxin which reaches and may continue to reach the central nervous system. When only a small amount reaches the spinal cord there may be only local contraction of muscles in the region of the wound. When larger quantities pervade the nervous centres there is sustained generalized contraction of muscles, involving particularly the masseters, the muscles of the spine, chest, and abdomen and to a less extent the limbs, recurring reflex clonic contraction of the muscles may occur but it is usually slight and of short duration. Massive absorption of toxin causes a greater excitability attended by the classical reflex spasms brought on by the slightest stimulation. In the severest cases they may be almost continuous and lead to fatality from cardiac or respiratory failure often preceded by hyperpyrexia (108°-110°).

In tetanus it has been observed repeatedly that the intensity of the

\* The incubation period may be as long as two months, especially if prophylactic immunization has been carried out previously.

disease (and its outcome) is closely related to its period of incubation, indeed, the incubation time is inversely proportional to the severity of the disease. Usually, too, in cases with a short incubation period there is an early onset of generalized muscle spasms which betokens an overwhelming toxæmia. From experience it has been found that when the incubation is under one week recovery is unlikely regardless of treatment.

## GAS GANGRENE AND ALLIED INFECTIONS

Gas gangrene is the most serious complication of wounds. It has a fatal outcome in 30% of cases. The onset is acute and the infection progresses rapidly. Usually the disease is manifested within 24 to 48 hours of wounding though in exceptional cases it develops within a few hours, and sometimes it is delayed for six or more days. Wounds of the buttock and lower limb are more often affected than those elsewhere and the outcome of the disease at these sites is more grave.

The organisms are anaerobic spore-bearing bacilli of the *Clostridium* group and are derived from the intestinal tract of man and animals. The pathological features of the disease are due to the powerful toxins produced by the organism and to their continued multiplication and spread in the tissues especially muscles.

In battle casualties gas gangrene is more prevalent in the winter months and in highly cultivated terrain than in the desert. Soiled garments are probably a frequent source of infection. In civil practice gas gangrene may complicate wounds contaminated with street dirt, manure and fouled clothing.

Generally several varieties of clostridia are responsible for the disease, though occasionally only a single species, e.g., *Cl. welchii* may be present. The chief species causing toxæmia are *Cl. welchii*, *Cl. septicum* and *Cl. admetiens*. The first two are locally destructive. *Cl. admetiens* has a longer incubation period (2 to 5 days) is less invasive but produces a very powerful toxin. In addition the wound may contain less pathogenic clostridia such as *Cl. sporogenes*, *Cl. tertium*, *Cl. bifermians* and *Cl. fallax*. When *Cl. histolyticum* is present in mixed infection the disease is almost invariably fatal. Concomitant infection of the wound with aerobic organisms such as streptococci, staphylococci, pseudomonas proteanæ and coliform bacteria is usual and may add to the gravity.

**Predisposing Factors.** It is very important to appreciate that clostridia are frequently present in wounds yet do not give rise to gas gangrene. The local factors in a wound which favour its occurrence are not fully understood. The chief known and suspected predisposing factors are —

- (1) Inadequate drainage or excision of deep penetrating wounds.
- (2) Involvement of muscle.
- (3) The presence of foreign bodies, devitalized tissue, or collection of blood clot.
- (4) Impairment of the circulation of the part, by damage to blood vessels or by constriction in tight bandages or plaster of Paris.
- (5) The presence of soluble calcium, derived, for example, from highly fertilized soil.

**Biological Properties of the Organisms** It is known that the special characters of gas gangrene depend upon the biological properties of the organisms concerned. All the organisms possess, in various degrees, the property of breaking down sugars and proteins, both of which are present in muscle. Some of the organisms, notably *Cl welchii*, are strongly saccharolytic, and these appear to play the dominant part in the infective process. Others, particularly *Cl sporogenes*, are strongly proteolytic, and their effect appears to be mainly synergic. Incidentally the proteolytic organisms are responsible for the gross putrefactive changes in the gangrenous part, and for the production of the peculiarly offensive gases.

In typical examples of gas gangrene due to *Cl welchii* and *Cl sporogenes*, it appears that *Cl welchii* initiates the process and proliferates more rapidly. It generates powerful toxins which spread rapidly in the long axis of the muscle and kill the muscle cells, and since the toxins are strongly hæmolytic the muscle becomes stained by liberated blood pigment, and assumes a characteristic brick red colour. In virtue of its saccharolytic properties the organism ferments the glycogen products, glucose and maltose, with the formation of acids and gases (carbon dioxide and hydrogen). This early rapid growth of *Cl welchii* is succeeded by the more gradual development of the proteolytic organism *Cl sporogenes*. The muscle in the neighbourhood of the wound, and later more distantly, undergoes putrefaction and becomes soft and diffuent, with the production of various organic alkalis and hydrogen sulphide and other noxious gases. As a result of combination of hydrogen sulphide with the iron set free from the blood by hæmolysis, the affected muscle acquires an olive green colour, and finally becomes black.



FIG. 5. Gas gangrene. Transverse section of a muscle at an early stage in the disease. The muscle fibres are separated by fluid exudate. A few polymorph leucocytes are present.

It is interesting to note that the acid produced by saccharolytic organisms such as *Cl welchii* tends to inhibit the growth of the organisms *in vitro*, but in wounds the acid is partly lost in the profuse discharge, and partly neutralized by inflammatory exudate, by calcium salts, and by the alkaline products of the proteolytic organisms.

**Types of Gas Gangrene** The onset and progress of gas gangrene vary greatly in different subjects. The infection is sometimes

fulminating and gas formation may be apparent within a few hours of the injury. In such cases the disease spreads rapidly, toxæmia is profound and a fatal issue not long delayed. This *fulminating type*, common in war wounds of the thigh is apt to occur when the blood supply of a considerable part of a limb is impaired. In less fulminating but nevertheless extensive infection, the gas formation may not be noticeable for 24 to 48 hours and then toxæmia is rather less rapid in development. In this type several muscles or even the whole limb may be affected (*massive type*). In the less virulent forms of gas gangrene seen more often in civil practice the infection is limited at first to a single muscle or a single group of muscles and these may become gangrenous from end to end although neighbouring muscles

remain untouched (*group type*). Less commonly, there is no involvement of muscle, and the infection is limited to the subcutaneous tissues and fascial spaces.

**The Pathological Changes** At first the affected wound has usually a dry surface later there is a thin exudate (sometimes sanious) containing fat droplets gas bubbles may be expressed from it. Organisms abound but leucocytes are scanty or absent. The wound at first emits a characteristic sweet odour. In the final stages the exudate is copious dark in colour and offensive. The sur-



FIG. 6. Gas gangrene. Transverse section of a muscle at a late stage in the disease. The muscle fibres are swollen and structureless and many of them have undergone disintegration. Note the absence of polymorph leucocytes.

rounding skin may be healthy or show mottling or greenish yellow patches in which large blebs may form. In an affected muscle the first recognizable change is a loss of contractility. Then the healthy colour is lost and gives place to a brick red discoloration. Later the muscle becomes yellow and friable and crepitates with gas bubbles, which are obvious at an early stage in X-ray films. Eventually it becomes soft and diffuent and its colour turns to olive green and finally black. It is noteworthy that the usual signs of inflammation and suppuration are absent.

The gas develops with great rapidity, and bubbles rise continually into the wound. At first the gas is odourless, and, from its content of hydrogen, is combustible. Later hydrogen sulphide and the other products of proteolysis give it a characteristic odour. The wound exudes thin blood stained fluid.

From the region of the wound the infection spreads in the long

axis of the muscle to its extremities but for a considerable time extension in other directions is limited by the muscle sheath. Eventually this is perforated usually alongside the nutrient vessels of the muscle, and the infection may then spread to other parts of the limb.

Microscopically the first change apparent, near the spreading edge of the infected area is that the muscle fibres are separated from their sheaths by an accumulation of fluid. This fluid is highly toxic, and by infiltrating in the long axis of the muscle and devitalizing the fibres it facilitates the spread of the infecting organisms. The muscle fibres, surrounded by the fluid, lose their striations and stain more deeply with eosin. Later the nuclei of the sarcolemma disappear and the whole fibre becomes necrotic. At a comparatively early stage the organisms are confined principally to the fibrous tissue reticulum of the muscle where they occur in large numbers. Later they invade the whole muscle.

**Constitutional Effects** The constitutional effects of gas gangrene result principally from the liberation of exotoxins, and only in the late stages do the organisms invade the blood stream. The toxins are principally hæmolytic and cause extreme anæmia with slight icterus. Extreme degenerative changes occur in the liver, kidneys and other parenchymatous organs. The liver may be infected in the terminal stages and becomes the seat of necrosis and gas formation (foamy liver). The adrenal glands undergo degenerative changes, and adrenalin disappears completely from the medulla.

### Anaerobic Streptococcal Cellulitis and Myositis

War experience brought to light an unusual but characteristic infection of the subcutaneous tissues and muscles caused by anaerobic streptococci with which are associated ordinary pyogenic organisms. It resembles gas gangrene, but differs from it in several important respects. It develops insidiously after an incubation period of 3 to 4 days with only mild systemic upset. In the wound there is usually a copious exudate and gas formation extending diffusely between muscle and fascial layers. The affected muscle is at first pale and boggy, next bright red and finally dark purple. It retains its contractile power. The skin usually shows intense erythema. The odour of the wound is less sweet and not so pungent as in clostridial infection. It is important to differentiate this type of wound infection bacteriologically from true gas gangrene because it is more likely to be survived and more conservative measures suffice for its relief.

### Progressive Post-Operative Gangrene of the Skin

An intractable form of infective gangrene of the skin and subcutaneous tissues may on rare occasions follow upon infected wounds. It has occurred most often soon after drainage of an appendix abscess or empyema. The gangrene appears several days or even a few weeks after operation. It involves the superficial tissues only and spreads slowly and progressively until very extensive areas are affected. At the spreading margin the tissues are raised, cedematous and under

mined and extremely tender. There is usually moderate constitutional disturbance.

The bacteriological investigations of this form of gangrene suggest that it may be due to combined activity of a micro-aerophilic streptococcus (a type common in the intestine and in lung abscess) and a staphylococcus in the skin. Fortunately these organisms usually respond to chemotherapy which has replaced the crude surgical measures formerly advocated.

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### CHAPTER III

#### CONSTITUTIONAL EFFECTS OF INJURY

THIS title includes hæmorrhage and burning as well as the condition known as traumatic shock, and in addition the special complication known as the crush syndrome

It is now established that hæmorrhage, burns and "shock" have many effects in common and they may conveniently be studied together. Each is associated with a circulatory disturbance, so it will be of advantage first to review some of the more important factors concerned in maintaining the circulation.

**The Mechanism of the Circulation** The circulatory system comprises the heart, the vascular bed (arteries, capillaries, veins) and the circulating fluid. In the traumatic disorders under discussion the heart's action is not impaired primarily, and indeed may be augmented to compensate for other defects. As a secondary development, however, the action of the heart may suffer, as a result either of anoxia or, when the venous return is insufficient, of impaired filling.

The arteries and veins also are not affected primarily, except perhaps in the acute reflex vasodilatation of syncope or "primary shock," and indeed in most traumatic circulatory disorders constriction of the arteries and veins goes a long way to compensate for the primary defect.

The capillaries, on the other hand, are affected very greatly. The capillaries, individually so minute, together form a network of vast potential extent. Normally only a small proportion of them are in active use and the remainder are contracted and empty.

Following trauma, the capillaries of the injured part are paralysed and dilate, while there may be a generalized capillary dilatation from anoxia or perhaps as a result of the absorption of depressor substances. Thus there results a disparity between the capacity of the vascular pathway and the volume of the fluid in circulation—a disparity increased by hæmorrhage or exudation of fluid into the tissues. It is this disparity which provides the key to the circulatory disturbance under consideration.

**The Capillary Fluid Balance** The fluid content of the body comprises the intravascular fluid (blood plasma), the interstitial or tissue fluid and the intracellular fluid. The volume of intracellular fluid is almost constant, for alterations outside a narrow range are incompatible with life. The intravascular and interstitial fluids, on the other hand, vary greatly in volume. Interchange of fluid between the blood and tissue spaces takes place at the semi-permeable wall of the capillaries and is dependent on the following physical factors—

(1) *The Capillary Hydrostatic Pressure* Thus, the "blood pressure" within the capillaries, is greatest at the arterial end and diminishes

towards the venous end. It varies in different capillaries and at different times, and also depends upon the level of the capillary relative to the heart, but in general it is of the order of 30 mm. Hg. at the arterial end, falling to about 20 mm. at the venous end. Its effect is to force fluid out of the capillaries.

(2) *The Osmotic Pressure.* The osmotic pressure exerted by the plasma proteins is roughly 26 mm. Hg. Against this there is the osmotic pressure exerted by the colloids of the tissue fluids, amounting to about 4 mm. Hg. Thus on balance there is a pressure of about 22 mm. Hg., having the effect of drawing fluid into the capillaries.

(3) *The Tissue Pressure.* This depends upon such factors as the filtration rate, the rate of lymph flow and the elasticity of the tissues. It amounts to a pressure of about 1-3 mm. Hg., tending to force fluid from the tissues into the capillaries.

Thus it will be seen that at the arterial end of the capillary the hydrostatic pressure exceeds the sum of the osmotic and tissue pressures, hence fluid exudes from the vessel; whereas at the venous end the position is reversed and some of the fluid is reabsorbed (the remainder draining into lymphatic channels). Following injury this mechanism is upset and, according to the nature and extent of the injury, water (crystalloid solution), plasma or whole blood may escape into the tissues and stagnate there.

### Fluid Loss

In different forms of injury the body may sustain an acute loss of water or plasma or blood. If the volume of circulatory fluid is sufficiently reduced a sequence of circulatory changes will occur independently of the character of the fluid loss. This sequence of changes will be considered later; first the differences depending on the character of the lost fluid will be studied.

*Dehydration.* Dehydration, by which is implied loss of either water or salt solution, is common in severe vomiting or diarrhoea or as a result of a combination of diminished fluid intake with loss by sweating or fistulous discharge.

In dehydration the blood undergoes concentration, as indicated by increase in the red cell count, haemoglobin index and haematocrit ratio. Moreover, the plasma protein content also rises, and in consequence the capillary osmotic pressure is raised and water is drawn from the tissues into the blood stream.

The transfer of metabolites between the blood and the body cells is impaired and thus causes anoxia. It thus seriously impairs the nutrition of such important tissues as the heart muscle, liver, kidneys and skeletal muscles. The changes differ somewhat according as the loss affects mainly water or mainly salt. In *pure water depletion*, such as results from dysphagia or from shortage of drinking water, the plasma and the tissue fluids become hypertonic and the urinary excretion fails. This does little harm (unless the loss is extreme) provided that the kidneys are healthy, for half a litre of urine then suffices to excrete the waste products; but if the kidneys are damaged uraemia will result.



*Mixed water and salt depletion* is the most common clinical type, for example in pyloric stenosis, in intestinal obstruction, duodenal fistula and severe diarrhoea. In addition to the features mentioned above there may be a disturbance of the acid base metabolism. In vomiting, where the loss principally concerns the chloride ion, alkalosis is apt to develop, in diarrhoea on the other hand, where sodium is lost in excess, there is a risk of acidosis.

*Pure salt depletion* occurs in diseases such as those mentioned above if the loss of water is made good, but insufficient salt is administered. It is important to recognize that if the loss has been great a salt deficit may persist even after the administration of several pints of physiological saline. Under such circumstances the clinical evidence of dehydration may seem puzzling but the true state of affairs can readily be recognized on estimation of the urinary chlorides.

**Loss of Plasma** Certain forms of injury, particularly burns, are characterised by loss of plasma from the circulating fluid. The blood is thus deprived of proteins and fluid while the cellular elements are retained. Examination of the blood therefore shows an increase in the red cell count, hæmoglobin index and hæmatocrit ratio, but a reduction in protein content. This latter feature is of great importance, for as the capillary osmotic pressure is reduced no fluid can be withdrawn from the tissues to make up the volume of blood in circulation. Indeed unless the protein content is soon restored by mobilizing reserves the fluid shift will be in the opposite direction and œdema will result with further reduction in the volume of the blood in circulation.

In plasma loss as in simple dehydration anoxia and acidosis will aggravate the disorder while in addition the great hæmoconcentration by increasing the viscosity of the blood will further impede the circulation.

**Hæmorrhage** When bleeding occurs rapidly and is copious the sudden acute loss of fluid from the circulation causes a sudden fall of blood pressure, which may be manifest in syncope or fainting. Very quickly, however, a compensatory mechanism is brought into action, which effects first (and almost immediately) a reduction in the capacity of the vascular bed and secondly (and more slowly) a restoration of the blood volume.

The reduction in capacity of the vascular bed is effected by vasoconstriction brought about by increased activity of the vasomotor centre, resulting from the fall in venous pressure and diminution in the depressor stimuli originating in the aortic and carotid sinuses. At the same time the heart rate is increased and its output thus somewhat augmented.

The restoration of blood volume is effected mainly by withdrawal of fluid from the tissues (a consequence of the fall of capillary hydrostatic pressure) and to a small extent by contraction of the spleen. Thus fluid replacement begins very soon after the hæmorrhage, but complete restoration of the blood volume takes many hours, or even days according to the amount of fluid available in the tissues or made available by timely administration.

This fluid readjustment has important secondary effects on the

composition of the blood. At first examination of the blood shows no departure from the normal, but soon there is evidence of dilution, as seen in diminution in the red cell count, hæmoglobin index and hæmatocrit ratio. Since full restoration of volume is slow, these estimations do not at first provide an accurate index of the amount of blood lost. There is also diminution in the protein content of the plasma, and if this is not rectified soon it will give rise to oedema.

In hæmorrhage, unlike simple dehydration and plasma loss, there is the additional factor of red cell loss, which by impairing oxygen transport increases the tissue anoxia. Since red cells are replaced slowly and hæmoglobin still more slowly the anoxia persists. This leads, in particular, to prolonged muscle weakness and especially to weakness of the myocardium.

**Late Effects of Fluid Loss.** Whatever the character of the fluid lost, unless the loss is rapidly made good there develops a sequence of events which tends to maintain and may increase the circulatory embarrassment. This sequence has been called the death cycle (McDowall).

The sequence is somewhat as follows. The reduction in volume of the circulatory fluid unless completely compensated by vasoconstriction leads to a fall of blood pressure and reduced blood flow. Consequently the venous return is reduced, cardiac filling is impaired, the heart, despite an increase in its rate, fails to maintain its output, and the blood pressure is further reduced.

In addition to this simple sequence there are several collateral developments which influence the "death cycle." The factor of increased viscosity of the blood has already been mentioned. Other factors are consequences of anoxia, which may be due partly (in hæmorrhage) to lack of hæmoglobin, partly to slowing of the blood flow and partly to deprivation of tissue fluids. Thus anoxia damages the myocardium. It also weakens the skeletal muscles—the second heart—and they fail to pump blood back along the veins. Most important of all, it impairs the nutrition of the capillary endothelium, increases its permeability and promotes the escape of fluid from the vessels.

### Traumatic Shock

The term "shock" has been applied to a wide variety of clinical states on no secure basis of pathology, and there are strong arguments in favour of discarding it. In this chapter the term is used merely as a convenient expression of the circulatory disorder resulting from injury.

In a typical case following a severe injury, the clinical progress is somewhat as follows. Immediately after the injury the patient collapses and may faint. This is the state of so-called primary shock. Although intense, this phase of collapse is not long sustained, and after a short time it may pass off completely. Later, generally within a few hours, signs of circulatory impairment reappear, the so-called secondary shock. This phase appears insidiously and if unchecked tends to progress and may prove fatal. At first the clinical signs are not definite. The patient is usually pale and limp and the pulse rate is somewhat rapid but the blood pressure may be normal or even raised. Only

later, when the compensatory mechanism begins to fail, do the classical signs of "shock" appear

It is now generally established that the early phase of syncope is the result of widespread vasodilatation, affecting both arteries and veins, with sudden fall of blood pressure. Thus vasodilatation is believed to be due to temporary paralysis of the vasomotor centre which is bombarded by painful and other afferent stimuli from the injured part, and perhaps also by stimuli from the higher centres.

The nature of the secondary circulatory disturbance has been the subject of numerous theories. It is accepted beyond all reasonable doubt that there is no primary heart failure (indeed the heart responds by increasing its rate and output) and no failure of the vasomotor centre (for compensatory arterial and venous constriction are obvious features) and that the primary and principal factor is disparity between the volume of blood in circulation and the capacity of the capillary network. It is accepted also that in the later stages the progress of the circulatory failure is along the lines described above as the "death cycle". The main field for controversy is as to the cause of the disparity between the blood and the vascular bed. As to this, the views held most widely at the present time may be summarised as follows —

(1) *Nerve Stimulation* We have seen that in the initial phase of syncope following an injury it is generally agreed that there is a transient paralysis of the vasomotor centre as a result of bombardment by afferent stimuli originating in the injured part. In the past, many workers have suggested that the later circulatory collapse has a similar origin, the result perhaps of sympathetic inhibition or perhaps of excessive secretion of adrenalin. It has, however, been shown that even when the state of "shock" is severe both arteries and veins are in a state of active constriction, from which it would appear beyond dispute that the vasomotor centre remains intact.

(2) *Depressor Substances* Cannon and Bayliss in experimental work on cats in which shock was produced by heavy trauma applied to the thigh found that the shock could be prevented by clamping the iliac vessels during the experiments but appeared after the clamps were released. From this they assumed that the circulatory collapse was due to the absorption of a toxic or depressor substance from the injured part. A few years later it was shown by Dale and Laidlaw that widespread capillary paralysis could be produced by injection of histamine, and thus arose the conception of shock as due to absorption of histamine like products from the damaged tissues. Later work, however, failed to confirm this hypothesis, for it was shown on the one hand that histamine shock is different in many respects from traumatic shock, and on the other hand that the histamine like substances produced in an injured limb are insufficient in amount to account for the collapse which may result. Interest in depressor substances as a cause of shock has however been renewed recently by the discovery that a substance obtained from crushed muscle possibly adenosine triphosphate, is capable of producing a shock like state. Such a factor may possibly explain why severe crush injuries of heavy muscles are particularly prone to shock.

(3) *Local Fluid Loss* After a severe injury the loss of blood by extravasation into the injured part may be considerable. In addition blood stagnates in the dilated capillaries of the part and, since the permeability of the capillary endothelium is increased plasma escapes from the blood stream into the tissue spaces. Earlier workers, while recognizing the existence of this local fluid loss, considered that it was not sufficient to account for the circulatory disturbance. According to Blalock and his colleagues however, the extent of the loss is greater than had been supposed. From experiments in cats in which, after traumatization of one thigh, the weight of the injured limb was compared with that of its fellow, he concluded that as much as half the total volume of blood in circulation may be lost in this way, an amount entirely sufficient to account for a severe degree of shock.

In man it is unfortunately not possible to assess the volume of fluid lost into the injured part. In burns, where a large amount of fluid exudes at the surface in addition to that which accumulates in the tissues round and deep to the burn it seems probable that this factor alone may be held responsible. In other types of injury the evidence is less convincing.

Whatever the nature of the primary factor in shock, clinical and experimental investigations in recent years have established many data of importance in relation to treatment, especially in relation to the three principal methods of treatment, rest, warmth and the administration of fluids. It is now realized that "rest" should imply strict immobility, for in the gravely injured patient even slight movements such as turning on one side gravely upset the blood pressure. The usual routine on admission to hospital of undressing and thorough cleansing may on occasions be fraught with danger.

The application of heat, formerly a cardinal principle of treatment, has also been shown recently to be dangerous if carried to excess. The blood vessels of the skin constitute a large part of the total vascular bed. In severe shock the skin capillaries are shut down—hence the characteristic pallor and coldness—and this should be regarded as a compensatory mechanism. The first effect of heat is to dilate these vessels and thus to increase the disparity between the blood volume and the capacity of the bed. Even in health, heat applied by a "shock cradle" for half an hour has been shown to bring about a notable reduction in the blood pressure.

Fluids may be beneficial or harmful according to their composition and rate of injection. The aim must always be to replace the type of fluid lost—blood plasma, saline solution or water as the case may be—but two special factors must always be borne in mind. First, it must be remembered that capillary permeability is impaired in the injured part and also perhaps throughout the whole body, and in consequence crystalloid solutions given intravenously will quickly leave the circulation. Moreover, since a certain amount of protein is carried out too the osmotic pressure is reduced and more fluid is lost into the tissues. Secondly, it must be remembered that while in the early stages it is desirable to replace the lost fluids rapidly, in the later stages rapid injection may be dangerous for if the venous pressure is raised too

quickly the heart muscle, impaired as a result of anoxia, may be over-taxed

### Burns

Burns or scalds differ from other forms of physical trauma in that they affect primarily one of the most vascular and richly innervated tissues of the body, they are usually extensive, and they are always prone to infection. It is not surprising, therefore, that the circulatory disturbance caused by burns differs in many features from that due to other injuries.

Immediately after burning there may occur a transient phase of collapse similar to the "primary shock" which follows other types of injury, and probably due similarly to reflex vasomotor paralysis.

The most characteristic phase occurs somewhat later, however, and becomes progressively worse during the succeeding two or three days. This phase, the so-called toxæmia of burns, has been attributed by different workers to a variety of causes, including suprarenal exhaustion, elevation of the blood potassium level, absorption of autolytic products from the burnt tissues, and sepsis. While the last two cannot be ruled out altogether—and indeed sepsis undoubtedly plays a part in some cases, though usually at a somewhat later stage—there is convincing evidence that the main factor concerned is loss of plasma.

This loss of plasma results from increased capillary permeability in the vicinity of the burn, some of the fluid accumulates in the tissue adjacent to the burn while there is a copious outpouring into blisters and as an exudation from the surface. It has been shown in animals that when the burn is extensive the fluid loss may amount to 60% or more of the plasma volume.

The blood changes follow naturally. There is marked hæmoconcentration, that is concentration of the blood cells as estimated by the red cell count, hæmoglobin index or hæmatocrit ratio. The protein content falls, and despite rapid mobilization from reserves may remain persistently below the normal. In some cases the reduction in blood protein is sufficient to induce generalized œdema. The potassium content of the blood may be raised, its significance is not understood.

While the importance of plasma loss is well established, it may not be the sole cause of the toxæmia of burns. Of other possible factors, the absorption of bacterial toxins is one of the most important. The risk of infection of a burnt surface is obviously very great, indeed it is almost invariable, despite the utmost care in treatment. Probably in most cases toxæmia resulting from infection assumes serious proportions at a somewhat later stage, i.e., two or three days after the injury, though exceptionally there is evidence to suggest that it may be a factor within 24 hours.

Still later in the course of a burn—usually after two or three weeks—a further constitutional upset occurs characterized by hypoproteinæmia and deficiency of hæmoglobin. It is especially apt to happen in an extensive burn. While it in part may be due to prolonged infection, its causation is not fully established. It is important not only for its

constitutional effects but also as a cause of delay in the healing of the burn

### The Crush Syndrome

This syndrome is characterized by renal failure developing as a complication of a crush injury to a limb. It is especially apt to occur when a limb has been pinned under falling masonry for several hours. The renal damage develops 24-48 hours after the onset of the injury. The urine is diminished in quantity, highly acid and excessively dilute, and contains pigmented casts and granular debris consisting mainly of myohæmoglobin derived from the damaged muscles. Azotæmia and acidosis ensue, complete anuria may supervene and death occurs commonly about the seventh day.

The changes in the crushed limb are characteristic. The limb is swollen, hard and paralysed. Arterial pulsation is absent at first, but may return, and as the circulation is re-established crops of blisters appear. Necrosis of the muscles is a prominent feature.

In the kidneys the microscopic appearance is that of an acute tubular nephritis, with selective changes in the ascending limb of Henle and the second convoluted tubule. Brown casts of myohæmoglobin are seen within the lumen. It has been suggested that the level of the lesion is determined by the acidification of the urine which takes place at this segment of the nephron.

The cause of the renal damage is not clear. Originally it was attributed to blockage of the tubules by myohæmoglobin but the microscopic feature of massive tubular necrosis and the dilute character of the urine are not to be explained on this simple hypothesis. It seems possible that ischæmia due to reflex spasm of the renal vessels such as has been shown by Trueta, Barclay and their colleagues to follow experimental application of a tourniquet to the lower limb, may play a part.

As a result of the renal damage, changes occur in the chemistry of the urine and blood. The urine is greatly diminished in quantity, is highly acid, and contains albumen and blood. Myohæmoglobin may be found within a few hours after release of the trapped limb. The blood urea and also the blood potassium rise steeply. The blood pressure is raised. Death from renal failure may occur with great suddenness.

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## CHAPTER IV

### TUBERCULOSIS

TUBERCULOSIS is one of the most widely distributed of all human diseases. All races are liable to infection and few escape. In Scotland the death rate had shown an accelerated decline during the last few decades, but in spite of immense improvements in preventive measures and treatment it is still about 77 per hundred thousand of the population, so that tuberculosis may be classed with venereal disease and cancer as one of the most important scourges affecting mankind.

Although tuberculosis in general comes within the domain of the physician, many of its local manifestations are at present regarded as within the scope of surgery. In the surgery of adults, tuberculosis of the lungs, the intestines, and the kidney and genital tract takes an important place, and in the surgery of children, tuberculosis of lymph glands, bones, joints, the peritoneum and meninges have a high incidence. It is thus evident that a knowledge of the pathological background of the disease is of importance to every surgeon.

**Frequency.** The most accurate method of assessing the true incidence of tuberculosis is by routine post mortem examination. This has been carried out by many workers in different parts of the world, and the recorded results are very instructive. Naegeli (Zurich) found that 71% of 500 bodies of all ages were tuberculous, and that amongst adults over 18 years of age 98% were definitely infected. Reinhart (Berne) recorded similar findings in a series of 360 cases. In Edinburgh, Todd, who conducted a thorough examination of 401 bodies, found that death was due to tuberculosis in 18, and that in 68.9% of the remaining 386, there were signs of tuberculous infection. In the Royal Hospital for Sick Children in Edinburgh (children under 12 years) Agnes Macgregor found in 1,127 autopsies (from 1922 to 1929) that tuberculosis, in some form, was present in 22% of cases, and that in no less than 18% it had been the cause of death.

Tuberculosis is a disease influenced notably by racial and economic factors, and these figures, which are from unselected communities in populous areas, indicate that the majority of adults and many children manifest some evidence of tuberculous infection, and that the lesion may be quiescent or progressive. The figures from children's hospitals show how frequently infection occurs in early life. This is of importance, because it is generally believed that the majority of people acquire a tuberculous focus (become tubercularized) before adult life, a belief substantiated moreover by the observation that the Mantoux skin reaction is positive in 50% of children under 12 years of age, in over 70% at 20 years. The primary lesion may either heal or form a focal point for extension of tuberculosis either immediately or much later. Although the initial or primary infection (usually in the lungs)



may be the starting point of progressive tuberculosis, more often active disease is the outcome of a fresh infection

**Resistance to Tuberculosis** Resistance to tuberculosis varies in different races, at different ages, and from time to time in the same individual. Usually infection acquired in the first two years of life is rapidly fatal from progressive lesions, an observation which emphasizes the importance of protecting young children from sources of massive or continuous infection. After the age of three years tuberculous infection, though more likely to be progressive than in older children, may remain quiescent or may even become arrested. In most civilized races there is a high resistance to tuberculosis, the result of progressive immunization during many generations, but in isolated communities, not previously immunized, the resistance is lacking. When members of such communities are subjected to infection they show an extreme susceptibility to disease, which may then take an epidemic form of great virulence. Very striking examples of this are provided by the behaviour of newly introduced tuberculous infection in communities in Africa, India, and elsewhere. The lungs are usually affected by a rapidly progressive pneumonial form of disease, which may assume an almost epidemic character. The death rate is about twenty times that present in peoples long protected by mild but continued exposure.

Infection early in life seems to have a partial immunizing effect, though it is insufficient to afford protection against massive superimposed infection in later life. Those specially susceptible to acute tuberculosis are young adults as yet unexposed to gross infection, and in whom the Mantoux skin reaction is negative. It is in such a group of subjects that protective immunization has been attempted and its need is obvious in such individuals as children of tuberculous parents, nurses and students in sanatoria, etc. Some degree of protection can be afforded by vaccination with living but avirulent and attenuated strains of bovine bacilli (B. *bilé*, Calmette Guérin, BCG). The practice long in vogue on the Continent and in Canada is to be adopted in Britain.

**Heredity and Tuberculosis** Congenital tuberculosis, the result of transplacental infection, is of great rarity. Recent observations have shown that in such cases the maternal uterus has been the seat of tuberculosis.

Statistical evidence is very conflicting in regard to the extent to which there is a specific *hereditary predisposition* to tuberculosis. The hereditary factor is important to the extent (as in other diseases) that some families have more than others tissues favourable for the survival of tubercle bacilli. Variation in susceptibility is dependent more on variation in environment than on specific susceptibility.

**Types of Infection** There are two common types of tubercle bacillus, the human type and the bovine type. The two are similar in appearance, and they can only be differentiated by culture or by animal inoculation. When cultured on glycerine egg medium the human type grows readily, producing in the course of two or three weeks an abundant wrinkled growth, whereas the bovine type grows hardly at all. When

inoculated into animals the bovine type is more virulent than the human type. An emulsion of 0.1 mgm of dried bacilli of bovine type injected intravenously in rabbits causes generalized tuberculosis and death within two months, whereas after a similar dose of the human type the animal dies only after two months, or may survive.

Both human and bovine types occur in man, and the frequency of each type varies in different organs and tissues. Bovine infection is generally regarded as more virulent, and more likely to give rise to multiple lesions or to generalized infection. With few exceptions intrathoracic tuberculosis at all ages is due to infection by the human type of bacillus, whereas, tuberculosis of lymph glands, bones and joints and the abdomen, especially in children, is due in a considerable proportion of cases to the bovine organism. In Glasgow, Blackburn found that in children up to thirteen years bovine infection accounted for 64% of cervical gland tuberculosis, 80% of abdominal, and 31% of bone and joint tuberculosis.

Griffith (1932) gave the following results of his investigations of the incidence of bovine infection in the principal forms of "surgical tuberculosis" —

Site of Disease	All Ages		0 to Four Years		Five to Fourteen Years	
	Number of Cases	Per cent. Bovine	Number of Cases	Per cent. Bovine	Number of Cases	Per cent. Bovine
Cervical lymph glands						
(England)	116	45.7	21	85.7	54	48.1
(Scotland)	114	73.6	53	84.9	71	74.6
Bones and joints						
(England)	520	18	88	27.3	351	18.5
(Scotland)	196	42.8	86	61.5	65	38.5
Genito-urinary						
(England)	23	17.4	—	—	3	33.3
(Scotland)	22	9.1	—	—	5	40.0

**Sources of Infection in Man** The most common sources of infection are (1) sputum from infected subjects, (2) contaminated milk from cows suffering from tuberculosis of the udder.

A phthisical patient may convey infection directly to those about him through his sputum or the sputum may become inspissated, and may then be carried by dust. In either instance infection may occur by inhalation or by ingestion.

Milk is a common vehicle for the tubercle bacillus, and so greatly is this source of infection dreaded in some cities that all milk is pasteurized before consumption. Improved veterinary and municipal administration has of late years reduced gradually the frequency of this source of infection, yet at least 7% of raw market milk in this country contains tubercle bacilli.

**Portals of Entry of Infection** Tubercle bacilli may gain access to the body by the mucous membranes or, rarely, by the skin. The skin reaction at the sites of the respiratory and alimentary tracts are uncommon. The commonest sites of entry of infection, and there need be no special point of the surface for its occurrence.

After Althou

Infected droplets of sputum or particles of dust may be inhaled so that bacilli reach the pharyngeal or respiratory mucosa which they penetrate. That bacilli may gain entry to the body by the pharynx is proved by the discovery of tuberculous foci in the tonsils of children, and it has been estimated that at least 5% of excised tonsils show evidence of tuberculosis. The mucous membrane of the trachea or of the bronchi also affords a surface for infection, and it is believed that catarrh of these passages favours its occurrence. Post mortem and radiographic examination in children has shown that



FIG. 7 Extensive calcification of tuberculous cervical lymph nodes

primary involvement of the lung (with secondary infection of the tracheo-bronchial glands) is by far the most common mode of infection—the so-called *primary complex*, or Ghon's focus.

The mucous membrane of the small intestine is the other great absorptive surface for tubercle bacilli, and the infection is almost always of bovine type carried by milk. Unlike most other organisms the tubercle bacillus, in virtue of its fatty capsule, can survive exposure to the gastric juice, even for a period of several hours, and thus reaches the intestines unharmed. The bacillus gains access to the tissues through the lymph follicles of the ileum, the most actively absorptive region of the gut. Sometimes local ulcerations of the mucosa are present, but usually the point of entry is not detectable.

Infection through a cutaneous surface is very rare, and is limited almost to those frequently in contact with infected material. It is consequently most apt to affect doctors, orderlies, or butchers. The organism gains access through an abrasion, and there sets up a

localized focus (*Mycobacterium tuberculosis*), usually situated on the hand, wrist or arm.

**The Early Evidences of Tuberculous Infection.** To begin with, tuberculosis is always a local disease, and it affects especially the

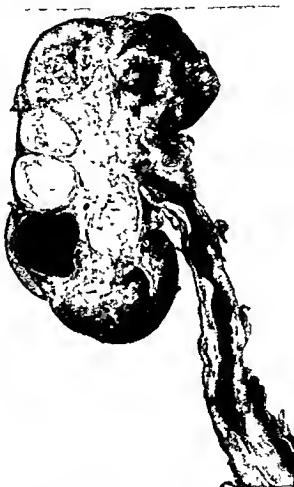


FIG 8 Tuberculosis of the kidney. At the upper pole there are two cavities, lined by tuberculous granulation tissue. At the mid part of the kidney there are masses of caseous material. Multiple small tubercles are present in the mucous membrane of the renal pelvis. The ureter is infiltrated and greatly thickened.

(Department of Surgery, University of Edinburgh.)

lymph vascular system of the body. It is therefore in the regional lymph glands and vessels draining the pharynx, lungs and small intestine that one seeks evidence of early infection. The initial foci of tuberculosis are usually found at one or more of the following sites: (1) the tonsils, (2) the cervical lymph glands, (3) the tracheo bronchial glands (by far the commonest), and (4) the mesenteric glands. From

the group of glands first involved the infection may spread to others. The affected glands may show little or no macroscopic evidence of disease, but usually one or several glands become enlarged, and may caseate. Later in life, if resistance proves adequate, the only evidence of former tuberculous infection may be calcification of a gland, and such hard nodules are often noted in the mesentery of the small intestine, the lung roots, and less often in the neck (see Fig 7).

**Progress and Spread of the Disease** The progress of tuberculous infection depends on the virulence of the bacilli and on the patient's powers of resistance.

In some subjects the original infection is followed by progressive tuberculous disease. In the vast majority the resistance proves adequate, and the organisms are either destroyed or entrapped in scar tissue. In others again the infection may remain latent during many years, and may later become reactivated and spread, if for any reason the resistance is lowered.

Natural resistance is low in the first few years of life, but becomes greatly increased in later childhood. The resistance may be undermined by malnutrition, intercurrent illness, or unhealthy environment, or by a combination of these factors.

The disease may spread in any of the following ways —

- (1) By the lymph vessels
- (2) By the anatomical passages.
- (3) By the blood

(1) *By the Lymph Vessels* This is quite the most important mode of spread in the early stages of tuberculosis, which is primarily a disease of the lymphatic system. From the lymph glands earliest involved, in the neck, mediastinum or mesentery, the disease spreads first to adjacent glands of the same group, and later to glands of other groups. Further extension by lymph channels or by apposition leads to the infection of other tissues and of viscera. From the mesenteric glands extension to the subserous lymph channels may cause tuberculous peritonitis. Spread from the abdominal lymph vessels to the thorax is sometimes noted, and this may occur along the line of the internal mammary vessels. In the thorax the disease may spread from the glands at the hilum of the lung to the peribronchial lymph vessels and to the lung and pleura. In the neck the glands on both sides may be infected, and from there the disease may spread to the mediastinum or the axilla.

(2) *By the Anatomical Passages* The most striking example of this method of spread is seen in tuberculosis of the larynx and of the intestines in phthisical patients, for it is generally accepted that these lesions are the result of infection from coughed up and swallowed sputum. A similar method of spread is witnessed in the lungs, where bacilli gaining access to the lumen of a bronchus from an ulcerating lesion may be responsible for extension elsewhere in the lungs.

It is said also that infection from a tuberculous kidney may be carried in the urine to the bladder, and it seems more probable that infection along the ureter spreads by contiguity of tissue rather than within the lumen.

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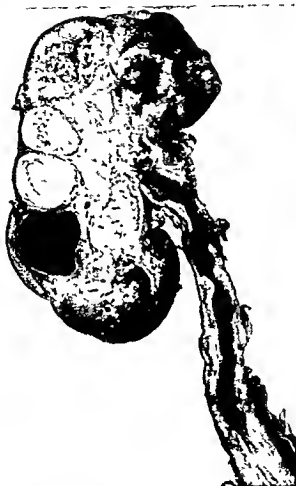


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(3) *By the Blood* The blood stream is an important channel for the spread of tuberculosis to the viscera. The bacilli may reach the blood stream as a result of ulceration of a venule in an infected lymph gland or in an ulcerative process in the lung or other viscus.

The visceral manifestations of tuberculosis—e.g., in bones and joints, kidney, epididymis, etc.—are believed to be due to dissemination via the blood stream. It seems probable that an active primary lesion in a gland or in the lungs may disperse showers of organisms into the blood stream from time to time. Many organisms are doubtless destroyed, but they may take root and lead to single or multiple tuberculous foci in the tissues in which they lodge. In this way may originate a solitary focus in one kidney or a bone or joint. If on the other hand, a large number of blood borne organisms survive they give rise to multiple foci in many tissues and viscera and thus lead to the condition known as *acute miliary tuberculosis*. In rare instances miliary tuberculosis assumes a chronic form and is sometimes survived. Chronic miliary tuberculosis affects particularly the lungs which are the seat of innumerable fine caseous deposits. The disease may persist for many months or years and may recover without residual changes. In a large proportion active tuberculosis develops elsewhere at a later date especially in bones and viscera, particularly the kidney. There is evidence that sarcoïdosis with its diverse mani-



FIG. 9 Tuberculosis of the epididymis. Both globus major and globus minor are enlarged and contain numerous caseous foci. The ductus deferens is thickened and nodular. The body of the testis is affected.

(Museum of Royal College of Surgeons of Edinburgh.)

festations is an atypical form of chronic miliary tuberculosis.

**Elimination of Tubercle Bacilli.** Tuberculous Bacilluria. Tubercle bacilli may be excreted in the urine in cases of active tuberculosis of the lungs, bones and joints lymph glands etc. The bacilluria is usually symptomless but there are always pus cells in the urine. The bacilli are not eliminated from the kidney by a process of simple filtration from the blood, but originate in minute and usually microscopic foci situated close to the cortical glomeruli. The small foci in the kidney are usually non progressive and after a variable time,



undergo fibrosis, but, in a few cases, renal tuberculosis may develop at a later date

In the same way, tubercle bacilli may be present in small numbers in the cerebrospinal fluid without evidence of meningeal origin. They originate from small overt foci in the brain substance.

**Relative Resistance of Organs and Tissues to Tuberculosis** It is a commonplace that certain organs and tissues are especially susceptible to tuberculosis, others relatively resistant. Lymph glands, the lungs, the intestinal tract and peritoneum, bones, joints and bursæ, are commonly affected, whereas the thyroid, heart and skeletal muscles are almost immune.

In some organs and tissues the resistance continues even after the disease has established itself locally, whereas in others it diminishes once the disease has gained a foothold. The lung shows definite evidence of resistance as indicated by fibrosis even when extensively diseased, whereas the meninges once involved show no such reaction. The behaviour of the kidney is paradoxical, for it may eliminate innumerable bacilli during long periods and yet remain relatively unharmed, but when once it becomes the seat of tuberculosis it undergoes extensive destruction, and rarely heals. Similarly the suprarenal gland is affected seldom, but when involved exhibits poor resistance, and its fellow often becomes infected.

**The Local Lesions of Tuberculosis** The characteristic lesion of tuberculosis, *i.e.*, the local reaction of the tissues to the presence of tubercle bacilli, is the tubercle or tuberculous follicle. Such a follicle consists of endothelioid (epithelioid) cells and lymphocytes, collected in a more or less spheroidal mass around a clump of bacilli. The endothelioid cells, which occupy the central parts of the young follicle, are oval or spindle shaped cells with faint staining nuclei and abundant clear cytoplasm. They are believed to be derived from the endothelium of blood and lymph vessels and from the fixed connective tissue cells of the part.

The lymphocytes, which are believed to be derived from

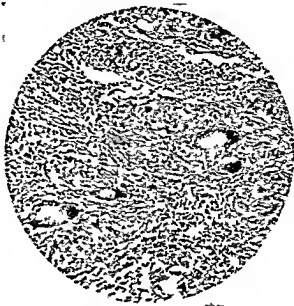


FIG 10 Section of a tubercle (low power). In the centre there are endothelioid cells and giant cells, while above and below there are collections of lymphocytes. There is no caseation.

the proliferation of focal perivascular lymph aggregations, are generally arranged in a more or less circular zone near the periphery of the follicle

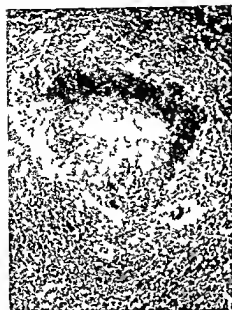


FIG 11 Section of a tubercle (low power). A typical tubercle is seen with central area of caseation surrounded by lymphocytes and endothelial cells. Two giant cells are evident.

tuberculosis. They are not, however, invariably present nor entirely pathognomonic of tuberculosis.

The above description is that of a tubercle in the earliest stages of its development, a tubercle which from its smallness may be described as a *miliary tubercle*. Very soon after its formation, however, the tubercle undergoes further changes and the first and most important of these is caseation. This is a form of coagulation necrosis affecting the endothelioid cells near the centre of the tubercle, and it is now generally attributed to the action of toxins set free from the bacilli around which the tubercle has formed. The endothelioid cells affected in this manner become swollen and lose their outline, their nuclei become faint and disappear and eventually the cells fuse in a dry, homogeneous mass of *débris* which from its naked eye resemblance to cheese is known as caseous matter.

From its inception a tubercle is completely devoid of blood vessels. This avascularity is attributable to the action of the bacillary toxins, which effect a necrosis of the capillary walls and an obliterative endarteritis in the larger vessels of the surrounding tissues and it is of special significance in that it tends to prevent the access of organisms to the blood stream.

Further changes in the tubercle depend upon the virulence of the disease and upon the reaction of the tissues. If the disease does not progress the tubercle becomes surrounded by fibrous tissue and may

Another constituent of the typical tuberculous follicle is the giant cell. This is a large cell of irregular shape, and often ill-defined at its margin. It contains numerous small oval or rounded nuclei, which typically are situated near one edge of the cell or are disposed in horseshoe formation. Commonly one or more such giant cells occur in a single follicle, and they are usually situated near the margin of the region of endothelioid cells. They are believed to be derived from an endothelioid cell in which amitotic division of the nucleus has been unaccompanied by corresponding cleavage of the cytoplasm. They are regarded as foreign body cells of special type, and when present in cellular collections such as have been described they are very characteristic of

ultimately become almost obliterated in a dense scar. Such "healed tubercles" are common in the lungs and in lymph glands. Frequently they undergo calcification, and are then recognizable in radiograms. If, on the other hand, the disease progresses, new tubercles develop in adjacent lymph tracts, and by confluence they may form foci of large size.

Occasionally, as for example in the meninges or, rarely, in a joint, the disease may progress with great rapidity from the onset, and the microscopic appearance may be that of an acute inflammation, with an exudate of fibrinous fluid and an infiltration of polymorph leucocytes (*acute tuberculosis*). Much more commonly, however, the course of the disease is slow and tractable, and is marked by a fairly even balance between the invading organisms on the one hand and the resisting tissues on the other (*chronic tuberculosis*). At the margin of a focus the process slowly extends its path partly barred by fibrous tissue derived from the surrounding stroma, whilst at the same time the central zone of caseation gradually enlarges sometimes to such an extent that entire organs, e.g., the kidney and the suprarenal gland, become completely caseous.

In certain situations, notably in bones and lymph glands, the caseous material is apt to undergo softening, and, by admixture with polymorph leucocytes to become caseous pus, forming a cold abscess.

**Hypertrophic Tuberculosis** In the ileocaecal region, in joints, and rarely in the stomach, the tissue response to tuberculous infection does not result in typical follicles but takes the form of a diffuse overgrowth of granulation tissue and young fibrous tissue, the so called hypertrophic form of tuberculosis. Microscopically, caseation is lacking, and giant-cell systems are scanty or even absent. In the ileocaecal region this form of tuberculosis leads to great thickening of the wall of the gut, and subsequently the contraction of fibrous tissue causes much narrowing of the lumen and binds the caecum, appendix and ascending colon in a firm shrunken mass. In joints the synovial membrane is replaced by a proliferating mass of granulation tissue which spreads in the form of a pannus over the articular cartilage and fills the recesses of the joint.

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## CHAPTER V

### ACTINOMYCOSIS

ACTINOMYCOSIS is a disease resulting from infection by the *streptothrix actinomycetes* and the lesions to which it gives rise belong to the group of infective granulomata. It affects especially the mouth, abdominal organs and lungs and is characterized by the formation of much granulation tissue and by fibrous infiltration and multiple abscesses. The disease is common in cattle and is by no means rare in man.

Pin head granules greenish-grey in colour though sometimes bright yellow like grains of sulphur, can usually be found in the invaded tissues or in the pus. These granules are compact colonies of the streptothrix, which grows as a mycelium or felted mass of branching filaments (hence the term 'ray fungus'). Occasionally the filaments are fragmented into bacillary or coccoid forms and occasionally there are rows of oval or spherical spore-like structures or gonidia. The filaments are Gram positive, and grow only at about body temperature.

There are several types of *streptothrix actinomycetes* but the only type responsible for actinomycosis in man is the organism isolated by Israel and Wolff. The organism is a non acid fast anaerobic streptothrix. It has been isolated from the tonsils, carious teeth and alimentary canal of healthy persons, and the view is now held that one or other of these sites is the source of infection. In actinomycotic lesions the streptothrix is often associated with other bacteria, sometimes as a gross infection e.g., with *B. coli* but always in conjunction with a minute Gram negative organism—*bacillus actinomyces comitans*. The associated bacteria are believed to furnish favourable local conditions for the invasion of the streptothrix and its proliferation, probably as has been demonstrated in the case of the tetanus, by reducing the oxygen tension in the tissues to a limit which will allow the anaerobic spores to germinate.

Cultivation of the actinomycetes from pus is difficult because it is frequently contaminated by organisms which, on account of their greater viability, outgrow the streptothrix in culture media. The difficulty may be overcome by repeated mixing and shaking of the pus in saline. The actinomycotic granules sink on standing and may be seeded independently into culture media. The most suitable media are blood agar, glucose agar or serum agar, and cultivation is carried out aerobically and anaerobically. The colonies on agar plates are dull white and round with filaments radiating into the surrounding medium.

**Methods of Infection and Transmission.** The recognition, bacteriologically of different varieties of the streptothrix actinomycetes and the identification of the type specific for human and animal lesions has helped to dispel the uncertainties as to how infection may be acquired.

The older view of the mode of infection was that actinomycosis was

essentially a disease of persons who lived in rural areas, and that they acquired it from grain seeds in the same way as cattle. Support for this belief seemed to be afforded by the observation that people engaged in certain occupations, such as harvesters, dairy workers, and stable attendants, were prone to suffer from the disease, and that in a number of instances there had been a history that infection had followed abrasions of the mouth or tongue by grain husks or stalks, etc. But in contradiction of this exogenous source of infection there is no authentic record of transmission of the disease from man to man or from animal to man, and, furthermore, later evidence indicates that the incidence in country is no greater than that in town dwellers. The association of foreign bodies with the disease has probably been overstressed, and now there is conclusive evidence that the streptothrix may be a normal inhabitant of the oral cavity and gastro intestinal canal of man and animals, leading there a saprophytic existence until local tissue injury affords an opportunity for the organism to gain a footing. In support of the now accepted view of endogenous infection, it is known that the *actinomyces bovis* is a very delicate organism which is not found outside the body and grows most readily if furnished with a limited supply of oxygen.

**Site of Infection** The commonest site of infection in man is the mucous membrane of the mouth or pharynx. The actual mode of infection is often doubtful, and it may be impossible to trace its source. Sometimes infection may be initiated by injury caused by foreign bodies or a dental extraction, but there is little doubt the frequency of the association of foreign bodies with the disease has been exaggerated.

In some instances the site of infection is the mucous membrane of the intestine, or, less often, of the bronchi. In rare cases infection of the skin and subcutaneous tissues has followed an abrasion.

**Characters of the Lesion** The affected area is infiltrated by a firm fibro cellular tissue. This may give rise to a hard, lumpy mass of chronic inflammatory material of brawny character with ill defined edges, or to multiple smooth nodules of uniformly firm consistence. One or more of the nodules may liquefy and discharge their characteristic granular and viscid necrotic contents. Healing of the sinuses may occur but is unusual while superadded infection persists.

**Mode of Spread** Unlike syphilis and tuberculosis, which it resembles in some respects and with which it is sometimes confused, actinomycosis spreads directly through the tissues. It does not usually attack the lymph glands, probably because the organism is too big to be carried by the lymph vessels. The disease begins in the submucous or subcutaneous tissues and travels in the fibrous tissue planes of the body. Muscles are pushed aside or infiltrated. Invasion of a vein is uncommon, but spread by the blood stream may account for metastatic lesions. Death in actinomycosis may be due to involvement of vital structures, generalized pyæmia, or to amyloid disease.

### ACTINOMYCOSIS AT SPECIAL SITES

Almost any organ of the body may be attacked by actinomycosis, but there are special sites at which it occurs. In over 60% of cases

the region of the jaws, tongue pharynx, and neck is affected, in about 20% the abdominal viscera, and in the remainder the thoracic organs. Sometimes there are multiple foci in various parts of the body

(1) Tongue, Jaw, Pharynx and Neck. A primary lesion in the tongue is rare, it usually begins at the margin of the organ in the form of a small deep-seated painless nodule which grows slowly. As the nodule approaches the surface the mucous membrane becomes stretched, and yellow areas corresponding to underlying abscesses, make their appearance. The condition in cattle known as "wooden tongue" was formerly ascribed to actinomycosis but is due to a specific actino-bacillus. Lesions due to this organism are exceedingly rare in man.

In man the jaws are the commonest starting point of actinomycosis,



FIG 12. Actinomycosis.

and the lower jaw is affected much more often than the upper. The disease often begins close to the angle of the mandible, and is often related to a carious tooth or an abrasion. Trismus may be an early sign. The lesion involves the soft tissues surrounding the jaws and the bone protected by its periosteum is not usually attacked directly, but the indurated tissues may be so fixed to the bone that an osseous origin of the disease may be suspected. The affected parts are firm and tough, diffusely swollen at first and nodulated later (see Fig 12). The disease spreads to the cheek and parotid gland and to the areolar tissues of the neck, in which it extends rapidly. In the neck, unless they are deep seated the lesions can be felt as firm nodules and the skin over them is often livid and puckered. As the nodules increase in size they soften to the degree of fluctuation and finally rupture, discharging sero-

purulent fluid and greyish or yellow masses containing the ray fungus, and leading to the formation of sinuses, which may intercommunicate. The skin, usually infiltrated and board like, varies in colour from pinkish red to dusky blue. The lymph glands are not involved unless there is a superadded infection.

From the neck the disease may extend to the mediastinum or to the vertebral column and the meninges. When the upper jaw is involved the disease may spread to the orbit or base of the skull and even to the brain.

(2) **Thoracic Organs** Actinomycotic infection of the lungs may result from aspiration or from extension of infection through the mucous membrane of the lower end of the œsophagus.

In a few cases primary pulmonary actinomycosis may be caused by direct aspiration of infective material from the upper respiratory tract, and metastatic lesions through the blood stream are said to occur.

The pathological appearances vary greatly, and three main types of lesion, which represent different stages of the process, are described. (1) The *bronchitic*, in which the infection is confined mainly to the large bronchi. (2) The *pneumonic*, in which the process spreads from the bronchi to the alveoli, which become filled with pus. (3) The *pleuro pneumonic* in which the abscesses have burrowed to the pleural surface and produced empyema. Often a considerable attempt at healing by fibrous tissue is evident, so that hard, fibrous nodules alternate with typical softer lesions or abscesses. The chest wall may be involved, and discharging sinuses may result. The brain may be involved by metastasis through the blood stream.

(3) **Abdominal Organs** Primary abdominal actinomycosis accounts for about 20% of all cases. The ileocecal region and the liver are most frequently attacked, less often the pelvic colon, and rarely the duodenum and the gall bladder.

The commonest starting point for actinomycosis is the ileocecal region, due to sudden or gradual escape of infection from a diseased appendix.

The disease is usually insidious in onset and chronic in course. It may become very widespread, and involve many of the abdominal organs by extension in the retroperitoneal tissues. It does not involve the peritoneal cavity. It may extend even into the thigh, and may involve the hip joint.

In a few cases abdominal actinomycosis has a sudden onset and may simulate appendicitis. At operation the appendix may be found to be involved in a mass of granulation tissue. When suppuration is present an indolent sinus may persist after operation, and become surrounded by vascular granulations and miliary abscesses. Sometimes at operation there is no palpable or visible mass, and the appendix appears healthy, and it is only subsequently, when the disease becomes more advanced and breaks through the wound, that its nature becomes obvious.

The *liver* is a fairly common site for actinomycosis. The lesion is sometimes a primary one, but more often is secondary to actinomycosis from the ileocecal region or even from the lung. In cases in which no

primary lesion is found in the intestine it is probable that the organism has reached a tributary of the portal vein through a small abrasion, or that the primary actinomycotic ulcer was small and has healed. The right lobe is the common site. It becomes enlarged and acquires adhesions with neighbouring structures. When cut the affected part has a very characteristic honeycomb appearance, probably due to coalescence of a group of abscesses, their contents have a rather bright yellow colour. Secondary infection of an actinomycotic abscess by pyogenic organisms is not unusual. Smaller abscesses may be present a short distance from the main one.

Actinomycosis of the liver may penetrate the diaphragm and infect the pleura and lung or it may involve the abdominal wall, giving the skin a characteristic board like hardness.

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## CHAPTER VI

### HYDATID DISEASE

HYDATID disease in man is caused by the *Echinococcus granulosus*. This is a cestode which normally completes its cycle of development in two hosts. In the *definitive host*—the dog—it takes the form of an intestinal tapeworm, the *tænia echinococcus*. This is a small worm, 3–6 mm. long, consisting of four segments (Fig. 13). Ova (known as hexacanthæ) set free from its terminal segment (proglottis) are evacuated in the fæces.

In the *intermediate host*—generally the sheep, less often the ox or pig—the ova derived from food contaminated by canine fæces penetrate the intestinal tract and are carried to the liver, where they lead to the

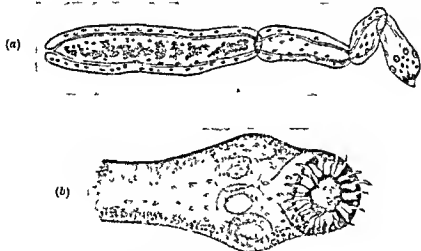


FIG. 13.

- (a) *Echinococcus granulosus*. Note the ova in the distal segment.  
(b) Head of *Echinococcus granulosus* showing suckers and hooklets.

formation of a hydatid cyst. Less often, secondary hydatid cysts may arise in the lungs or other sites.

Man, like the sheep, acts as an intermediate host. Probably in most cases the infestation is acquired in childhood as a result of contact with an infested dog.

**Geographical Distribution.** The disease occurs in all countries; but it is found with greatest frequency in those in which sheep are pastured in large numbers, because these animals act as the intermediate hosts for the parasite. On this account Australia, New Zealand, the Argentine, and South Africa, which are the great sheep-raising centres

of the world, show the highest incidence of the disease. In the State of Victoria in Australia it has been estimated by Dew that 1 per 800 hospital admissions is on account of hydatid disease. In Europe, hydatid disease is rare, although there are a few countries, such as Denmark, Northern Italy, and Iceland, where the disease has a relatively high incidence. In the British Isles few cases occur, and most of them are in Orkney, Shetland, and Wales.

**Development of the Hydatid Cyst** The embryo usually lies in one of the liver lobules, where its presence sets up a very active cellular reaction. An infiltration of the tissues with lymphocytes and endo-

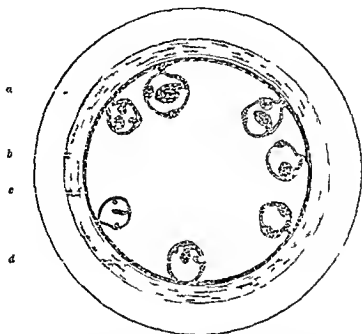


FIG. 14. Diagram of a fully developed unilocular hydatid cyst. *a*, adventitia or ectocyst; *b*, laminated membrane; *c*, germinal layer; *d*, brood capsule with scolices. (Modified from Dew.)

thelial cells as well as with erythrocytes occurs, and the specific response to the helminthic toxin is evidenced by eosinophilia.

About fourteen days after implantation the parasite assumes a vesicular form, and at this stage four zones may be observed. In the centre is the vesicular embryo, surrounded by a layer of endothelial cells, around which are concentrically arranged fibroblasts, and, at the periphery, a few layers of degenerated liver cells. By the fourth week the cyst is quite recognizable by the naked eye, and by the third month it may be several centimetres in diameter.

**Structure of the Mature Cyst** The fully developed cyst is lined by a membrane, variously known as the *endocyst*, *granular*, *parenchymatous*, or *germinal layer*, composed of small nucleated masses

embedded in granular protoplasm, from the inner aspect of which project the *brood capsules and scolices* (see below). The lining membrane is very loosely attached to the subjacent *laminated layer*, which is firm and serves to protect the delicate germinal layer and its developing scolices. The laminated membrane is very impervious to noxious agents. The outer coat or *ectocyst* or *pericyst* is an adventitious capsule formed from the tissues around the cyst, and is therefore, not an integral part of the parasite. It is composed of fibrous tissue and varies greatly in thickness. There is a definite line of cleavage between the laminated layer and the adventitious capsule.

In the interior of the cyst is the characteristic hydatid fluid, clear, and opalescent with an alkaline reaction. It acts as a nutrient medium for the developing scolices.

Brood capsules develop from the germinal layer and appear as small vesicles attached loosely to its inner surface. Scolices develop on the surface of the brood capsule at several points by a process of evagination and cupping of the proliferating capsule. A typical scolex is attached to the brood capsule by a fine stalk and swings freely within the capsule. The mature scolex has the typical shape of the head of the mature worm and the same arrangement of hooklets, which have a retractile mechanism to protect them from contact with their neighbours. Aggregations of them noted when a cyst is opened are known as 'hydatid sand' on account of the calcareous particles they contain.

A daughter cyst is a replica of the mother or primary cyst within which it occurs. It generally develops when the vitality of the mother cyst is endangered and thus represents a defensive mechanism for the larval cestode. Daughter cyst formation may follow injury, infection, or the entry of noxious fluids into the cyst, but is rarely observed in childhood, or in cysts in such sheltered sites as the brain and bones.

#### PATHOLOGICAL FEATURES OF HYDATID CYSTS

Hydatid cysts have been observed in almost every organ of the body, but the majority, as mentioned above occur in the liver or lungs.

The rate of growth of a cyst is very variable and depends on the tissue in which the cyst occurs. In soft vascular organs like the lung, spleen and brain cysts grow rapidly compared with cysts within the bones. The parasite may retain its vitality for as long as 40 years or it may die, spontaneously or as a result of rupture or infection of the cyst. In the early stages of its growth it usually gives rise to eosinophilia and this may recur if rupture, leakage or infection of the cyst takes place. If the parasite dies the cyst wall may become calcified and the contents pultaceous (*atheromatous cyst*).

As the fluid of a hydatid cyst is under considerable pressure, the cyst remains spherical and tends to grow in the lines of least resistance. Thus a cyst of the liver may become pedunculated, or may bulge into the retroperitoneal tissues.

As a hydatid cyst grows but slowly, pressure effects may be long deferred, for the affected structures have sufficient time to accommodate

themselves. In the liver the costal margin may bulge, or the bile ducts may be occluded. In the brain, signs of increased intracranial pressure may become evident.

In operations upon hydatid cysts, advantage is taken of the lack of cohesion between the laminated layer and the adventitious capsule to evaginate the cyst. To eliminate the risk of disseminating the disease, the contents of the cyst may be destroyed by injection of formalin. Excision of the cyst is unnecessary, although removal may conveniently be carried out if the cyst be pedunculated.

**Hydatid Anaphylaxis.** Rupture or leakage of a hydatid cyst may occur spontaneously or as a result of puncture or other surgical interference. After rupture, especially if the patient has previously been sensitized by minor leakage from the cyst, anaphylactic phenomena, mild or severe, may occur. For this reason exploratory puncture of a cyst is a particularly injudicious practice.

The anaphylactic phenomena vary from pruritus and urticaria or a feeling of constriction in the chest, to serious symptoms such as convulsions, pulmonary oedema or syncope. General anaesthesia mitigates the effects of anaphylaxis, but their manifestations may be delayed until after recovery from the anaesthetic. The sensitization resulting from repeated absorption of protein from hydatid fluid is utilized for two diagnostic measures, the complement fixation test and the intradermal reaction (of Casoni). The test is positive in 70%.

#### HYDATID CYSTS IN SPECIAL SITES

(1) **Liver.** As the ova of the *tænia echinococcus* are conveyed by the portal circulation it is not surprising that at least 75% of all hydatid cysts affect the liver, and when hydatids are present in other organs such as the lungs, the liver is affected in a high proportion. This is a consideration of great importance in prognosis and treatment.

In the liver hydatid cysts tend to develop in young subjects, though they often remain latent. The right lobe is more commonly affected than the left in the proportion of about 4 : 1 and when the cysts grow to large size the unaffected lobe usually shows considerable compensatory hypertrophy. Cysts near the peritoneal surface of the liver tend to spread towards the abdominal cavity, those originating near the free border of the liver may become pedunculated. At the superior surface of the liver the cyst may cause elevation of the diaphragm, a feature recognizable by radioscopy. A cyst occasionally originates at the bare area of the liver, and may then extend into the retroperitoneal tissues.

In adults, daughter cysts are present in fully 90% of cases as a result of irritation caused by the entry of bile.

The majority of hydatid cysts in the liver remain latent. Ultimately the parasite dies and the cyst wall undergoes calcification. In a small proportion complications occur, of which the chief are (a) suppuration, and (b) rupture.

(a) In a univesicular cyst the laminated layer is impermeable to organisms, therefore suppuration only occurs after communication with the bile passages. The common infecting organisms are *bacillus coli*,

streptococci, and staphylococci, but sometimes gas producing organisms are present

(b) The cyst may rupture into the biliary passages the peritoneum, the pleura and lung or rarely into an abdominal viscus

If the cyst ruptures into the biliary passages, obstructive jaundice may result, or daughter cysts may be discharged and may be discovered in the stools. Rupture into the peritoneal cavity may give rise to severe anaphylaxis, and later to the development of multiple

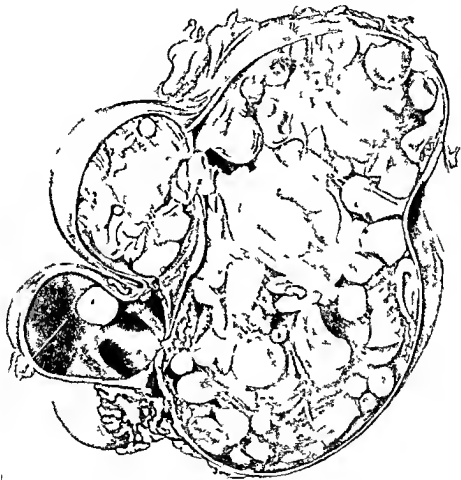


FIG. 15 Hydatid cyst of the kidney causing hydronephrosis  
(Museum of Royal College of Surgeons of Edinburgh)

daughter cysts. In some cases the rupture leads to extravasation of bile and to an early fatal issue.

Rupture into the thoracic cavity is usually a complication of suppuration of a large cyst, especially one situated in the upper part of the liver, on the right side. Empyema is the natural result, but sometimes rupture occurs directly into the lung which has become adherent to the suppurating cyst. As a result the contents of the cyst together with bile may be expelled into a bronchus.

Rupture of a hydatid cyst into the stomach the small intestine, and the colon has been recorded. Such complications are rare and are usually sequelæ of suppuration.

(2) **Lungs** After the liver, the lungs are the commonest site of echinococcal cysts and the possibility that a pulmonary and a hepatic cyst may coexist should not be overlooked. The usual route by which the parasite reaches the lungs is by the blood stream *via* the liver.

The right lung is affected twice as often as the left, and the lower lobe is the common site. As a rule the cyst arises near the surface of the lung (peripheral cyst) much less often near the hilum (para-bronchial cyst). Occasionally the cysts are multiple.

The lung tissue is non resistant and therefore pulmonary cysts grow relatively quickly and daughter cysts are not present until a late stage. The laminated membrane and the adventitious capsule are usually very thin especially while the cyst is univesicular and uncomplicated. Brood capsules with scolices (hydatid sand) are almost always present.

A peripheral cyst is usually attached to the parietal pleura by light adhesion, which following infection may become firm and widespread. A pulmonary cyst may rupture into a bronchus or into the pleural cavity, or it may become infected and lead to abscess formation in the lung or to pyopneumothorax. Rupture into a bronchus is an occasional event, and albuminous fluid, or the membrane of daughter cysts may be expectorated and natural cure may follow. By pressure a hydatid cyst may be responsible for secondary changes such as bronchiectasis. Following removal of a hydatid cyst failure of cohesion of the walls of the pericyst is liable to occur so that a cavity liable to infection persists in the lung. It is for this reason that removal of the portion of lung containing the cyst is to be preferred.

(3) **Brain.** Hydatid cysts in the brain are rare. The cyst is single and unilocular, it is seldom larger than a hen's egg and its adventitious capsule is very thin. Any part of the brain may be affected but the commonest site is one of the cerebral hemispheres superficially. The cerebellum is rarely involved. In children the skull bones may bulge over the surface of the cyst, but in adults they are more rigid and merely show thinning at the point of contact of the cyst. The cyst may deform, and finally rupture into the ventricles of the brain.

In the brain a hydatid cyst grows very slowly, and is therefore for long symptomless. The effects produced by the cyst vary according to its situation and are similar to those caused by benign tumour. A single cyst is readily amenable to surgical removal.

(4) **Kidney** Even in places where hydatid disease is common, renal hydatid cysts are rare, and when they occur seldom produce very definite signs. They may reach an enormous size without producing any important complication. Occasionally the cyst ruptures into the renal pelvis and may then become infected. Hydatid membrane, or even daughter cysts, may be passed in the urine, with symptoms of ureteral colic or urethral obstruction.

(5) **Bone** This is one of the rarest sites for hydatid disease. The

bones which have been most often attacked are the humerus, the femur, the vertebræ, the tibia, and the innominate bone. As hydatids in bone grow very slowly, they are usually recognized only in adults.

The unyielding nature of bone modifies the normal evolution of the cyst, so that localized solid masses of hydatid material like grains of boiled sago gradually replace the marrow and osseous tissue.

The outstanding feature of hydatid cysts in bone is their extreme latency. In situations like the femur or humerus, spontaneous fracture is often the first indication. Such pathological fracture is a grave complication, not so much on account of the improbability of union, but because it leads to dissemination of the disease in the soft tissues. Radiographically, hydatid disease in bone may be almost indistinguishable from osteitis fibrosa.

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## CHAPTER VII

### TUMOURS

TUMOUR formation, its nature and causes its relationship to other diseases its prevention control are problems of great perplexity, which have in turn attracted and baffled most who have studied them. The problem of new growth holds many disappointments for those who attempt to probe its mysteries and many forsake it for more promising fields but nevertheless it remains one of the most fascinating subjects in the whole realm of pathology.

Powell White has defined a tumour as "a mass of cells tissues or organs resembling those normally present in the body, but arranged atypically which grow at the expense of the organism without, at the same time, subserving any useful purpose therein." The most striking attribute of all tumours is their complete autonomy. A tumour is derived from the cells of the body in which it grows, it is as much an integral portion of the body as the liver or kidney or any other organ, yet it recognizes no laws except its own, proceeds independently, and often encompasses the destruction of its host.

The autonomy of a tumour is demonstrated by the manner in which it exacts nourishment regardless of the state of nutrition of the victim. It is like a mutinous army devastating its own country, for, however impoverished the host the tumour continues to flourish.

One of the few favourable features of even the most malignant tumours is their local origin, and it is upon this that the whole treatment of cancer by surgery is founded. It is probably not true that a tumour always starts from a single atavistic cell—in the breast, for instance, the origin is probably multicentric—but nevertheless it is correct to assume that in the majority of cases a tumour at its inception is localized. Simple tumours remain localized indefinitely, and many malignant tumours remain so for a period measured in months or years. A few, however, such as certain types of melanoma spread rapidly to other parts so that secondary nodules may appear even before the primary growth is recognized. In other cases, multiple primary malignant growths may appear, simultaneously or in succession. They may occur in different parts of the same organ, in paired organs or in different parts of the body,

### SIMPLE AND MALIGNANT TUMOURS

Between typical simple and malignant tumours there is little in common except their autonomy and the distinction can usually be made with ease on either clinical or pathological examination. Other tumours however, possess some of the features of both classes, and are not easily assigned to one or other, whilst yet other tumours change their



nature in the course of years, and, after a period of simple growth, undergo malignant change

The distinction between simple and malignant tumours is consequently not always possible, but in general it can usually be settled by the following criteria —

(1) A simple tumour usually attains a limitation of growth, and after reaching a certain size ceases to progress or at least progresses more slowly. A malignant tumour, on the other hand, grows continuously, and, even when it has impoverished its host and source of nutrition, it still retains the potentiality for further proliferation.

Illimitable growth is seen in malignant mouse tumours which, if suitably transplanted from animal to animal, continue to live and grow long after their first host is dead. Jensen's mouse tumour arose spontaneously in a white mouse in the year 1900, has since been conveyed from mouse to mouse in many laboratories throughout the world, has

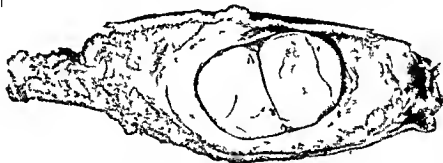


FIG 16 Pericanalicular fibro-adenoma of the breast, removed from a woman aged twenty eight years. The tumour had grown slowly during several years. It is non malignant and is surrounded by a well defined capsule of condensed fibrous tissue.

(Department of Surgery University of Edinburgh)

produced during that time innumerable large tumours which together must be many million times the weight of the original mouse, and thirty years later (ten times the mouse's span of life) was still growing actively.

(2) Usually a malignant tumour grows rapidly, a simple one slowly. To this, however, there are many exceptions, some simple tumours grow more quickly than cancers, and few malignant ones grow more quickly than that most innocent of "tumours," the foetus.

(3) Malignant tumours invade and destroy neighbouring tissues and possess no effective capsule. Simple tumours merely expand, and consequently are sometimes encapsuled. The gloma, however, has no capsule, though in the pathological sense it may be non malignant, and there are other exceptions to this general rule.

(4) Malignant tumours readily ulcerate upon free surfaces, by invading the surface membrane and interrupting its blood supply. Simple growths rarely ulcerate unless they undergo necrosis or suppuration.

(5) Malignant tumours tend sooner or later to disseminate and form metastases, and unless treated early and radically they almost invariably kill simple tumours rarely cause fatality unless they interfere with the function of vital organs.

**Microscopic Appearance** Microscopically, the nature and degree of malignancy of a tumour may be judged on three distinct criteria: (1) the relation of the tumour to its environment, (2) the structure of the tumour, and (3) the appearance of its cells. In general, the first criterion is most valuable, and for this reason it is important to examine the growing margin rather than the central parts. The most obvious evidence at the growing margin is the presence or absence of invasion of surrounding tissues, for with few exceptions malignant growths invade, simple ones do not.

In regard to internal structure of tumours, the striking feature is that simple tumours tend to repeat with some degree of accuracy the

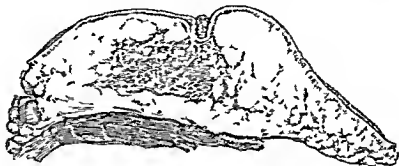


FIG 17 Scirrhus carcinoma of the breast. The tumour possesses no capsule and has infiltrated the tissues of the breast. The nipple is deeply retracted.

(Department of Surgery University of Edinburgh.)

pattern of the tissue from which they are derived, whereas malignant tumours reproduce the tissue very imperfectly or not at all.

The appearance of the individual cell of a simple tumour may be hardly distinguishable from the normal, but in typical malignant growths the cells have several strikingly abnormal features. In general, the malignant cell may be said to possess anaplastic characters and to approximate to an embryonic type. The principal function of an adult cell is to work, that of the embryonic cell is to multiply, and the more malignant the cell the more does it develop the latter function at the expense of the former. Typically, a malignant cell is larger than its prototype, is of irregular shape, and stains more deeply. The nucleus, which is a reliable guide to the state of activity of the cell, is hyperchromatic, and often of vesicular appearance. Mitotic figures are common in rapidly growing tumours, and often the mitosis is of irregular pattern. Sometimes there is a large densely staining spot quite distinct from the nucleus, the so-called "bird's eye spot." These spots have often been regarded as parasitic inclusions, but they are probably due to multiplication of the centrosomes in irregular cell-division. Another

index of rapid growth is the presence of "tumour giant cells," which must not be confused with other types of giant cell, such as occur in specific forms of tumour or around foreign bodies (see Fig. 80).

### GRADES OF MALIGNANCY

Attempts have been made to assess and grade the degree of malignancy of tumours according to their cytological pattern. Such an index of malignancy was formulated by Broders and was at one time adopted freely in America.

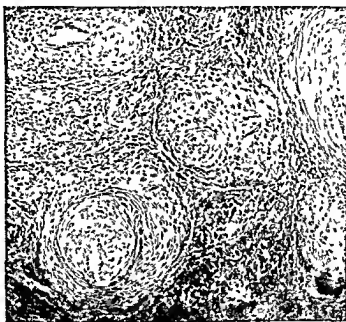


FIG. 18. Squamous cell carcinoma (epithelioma) of the tongue.  $\times 70$  The cells are highly differentiated, and some are keratinized. This tumour would correspond to type 1 of Broders' classification. Note the lymphocyte infiltration near the lower margin of the section, a common feature in lingual carcinoma.

This method differs from most others in that it relies entirely upon the microscopic appearance of individual cells of a tumour, and upon the degree of "de-differentiation" or reversion to the embryonic type displayed. Four grades of malignancy are recognized. If 75% or more of the cells are highly differentiated, the tumour is assigned to Group 1, the group of lowest malignancy. Group 2 contains those tumours with 50% to 75% of the cells differentiated, Group 3 with 25% to 50%. In Group 4 are those tumours in which the majority of the cells are "de-differentiated," and consequently includes the most malignant types.

Broders' method appears to be helpful when applied to such growths as squamous-cell carcinoma of the skin, tongue and lip, and

should not be regarded as generally applicable to all tumours. In assessing the malignancy of a tumour there are, of course, many other factors to be taken into account besides its histological grading. Such

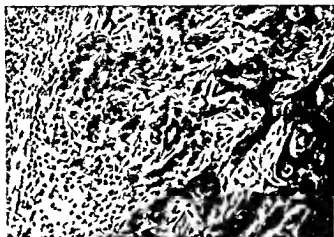


FIG 10 Squamous epithelioma of invasive type without keratinization or cell nest formation. This tumour would correspond to type 4 of Broders' classification.

features as the size and extent of the tumour, its position in relation to lymph drainage, its accessibility for surgical eradication, and its radio sensitivity, may all have to be considered.

### SPREAD OF MALIGNANT TUMOURS

Since the object of surgical operation in malignant disease is to extirpate all invaded tissues, the study of all the possible routes by which tumours spread is of immense practical importance. Indeed, the influence of such considerations upon the scope of the operative treatment is manifest in every region of the body.

A sarcoma differs from carcinoma in its method of extension. It infiltrates locally in much the same way, but sarcoma shows a great tendency to early dissemination by the blood stream, whereas carcinoma spreads first and principally along the lymph channels, and gives rise to blood borne metastatic deposits at a relatively late stage or not at all.

The spread of carcinoma, which is of greater surgical importance than sarcoma, will be considered in more detail. Carcinoma may spread in the following ways —

- (1) Invasion of adjacent tissues
- (2) Permeation and embolism in lymph channels
- (3) Embolism by the blood stream
- (4) Implantation of free cells

(1) **Invasion** Direct invasion of surrounding tissues is always the first mode of spread. Indeed, it is often difficult to assume that a tumour is malignant until it invades.

As the tumour invades it destroys the surrounding healthy tissues, probably in virtue of enzymes from the malignant cells.

A tumour does not invade uniformly, but its invasion is influenced to some extent by the disposition of fascial planes and other barriers. It seems that the invading cells take the paths of least resistance, and any tough membrane, especially if avascular, exerts a restraining influence. The pylorus forms a most remarkable barrier to the spread of tumours, and is rarely transgressed even by the most malignant gastric carcinoma.

Carcinoma like sarcoma, extends principally in connective tissues, but carcinoma may invade epithelial structures such as the skin and mucous membranes. For this reason a carcinoma, if superficial, commonly ulcerates early.

(2) **Extension by Lymph Vessels** Extension by lymph vessels often occurs early in carcinoma, and it provides the great obstacle to eradication of the disease by operation. There are two possible modes of spread within the lymph vascular system (a) by permeation, (b) by embolism.

Sampson Handley has vigorously sponsored the theory of permeation. According to him, the tumour, having once gained access to the lymph vessels, grows centrifugally in all directions in the form of advancing columns of cells, which permeate further and further from the primary growth. As the malignant cells at the head of each advancing column divide and progress the cells further back become obliterated by a fibrous peri lymphangitis. Consequently a centrifugal zone of spread a "malignant ring worm" results which increases progressively and reaches more distant parts of the body. At intervals some of the cells of this annular zone grow more actively and form visible metastases. Hence, in such a region as the breast, the earliest metastases usually lie close to the primary tumour, whereas those formed later lie at progressively greater distances.

In support of this view Sampson Handley has put forward many interesting observations, most of which relate to cancer of the breast, and are considered more fully in the chapter on that subject. The theory has not yet, however, received complete acceptance. Most authorities agree that spread by permeation does occur, but few are prepared to attribute to this process the predominant rôle that Handley claims for it.

Of the second process of lymph spread cell embolism there is no doubt. Small groups of cells set free in the lymph vessels are carried by the gentle lymph current to neighbouring glands where they are arrested in the subcapsular sinuses. By such a process glands comparatively remote from the primary tumour may be involved at an early stage and successful operation thus precluded. Conversely, carcinoma arising in tissues of which the lymph drainage is impaired by previous lymphangitis does not metastasize for months or even for

years. Lupus carcinoma, for example, rarely metastasizes until the primary growth has extended beyond the area of lupus and has thus reached patent lymph channels.

(3) **Dissemination by the Blood Stream** This usually occurs late in carcinoma, although there are exceptions. The lateness is partly due to the fact that in carcinoma the blood vessels are well developed and are not easily invaded by tumour cells, and partly to the fact that carcinoma cells which have reached the blood stream and have been deported to distant sites do not necessarily survive. Schmidt has shown that the lungs may contain many cancerous emboli, which have failed to engraft, and instead lie buried in fibrous capsules inside occluded blood vessels.

Blood borne metastases show a remarkable affinity for certain organs or tissues. The lungs, liver, brain and bones are commonly affected, whereas the muscles, heart and spleen are almost exempt. Some tumours commonly give rise to metastases in the liver and lungs, others *e.g.*, tumours of the breast, the kidney and the prostate, often metastasize to bones. These facts clearly indicate that the tissues differ in their susceptibility to cancerous invasion.

Malignant emboli from almost any part of the body are first arrested in the capillaries of either the liver or the lungs, and consequently the first blood borne metastases are usually in these organs. Occasionally, however, metastases arise in other regions without the lungs or the liver being obviously involved. According to Schmidt, malignant cells held up in the lungs, though unable to form pulmonary metastases, may proliferate along the pulmonary capillaries and reach the venules, and so may escape into the systemic circulation.

A tumour of rapid growth, with imperfect vessel walls *e.g.*, a hypernephroma or a bronchial carcinoma may be the source of a 'tumour embolus' composed of a mass of malignant tissue sufficient to lead to infarction within the part to which it is conveyed in the blood stream.

It has been suggested that carcinoma may spread by reversed blood flow within the veins adjacent to a tumour, the result of blocking by thrombosis or invasion of collateral channels (retrograde venous embolism). Such a process has been held responsible for the widespread extension of carcinoma of the prostate to the spine, pelvis etc., and for the extension of carcinoma of the breast and lung to distant sites.

(4) **Implantation of Free Cells** This mode of dissemination is seen most clearly in the peritoneal cavity. Cells from a tumour of the stomach, colon or other viscus may be set free and engraft on other parts of the peritoneum. The ovaries are commonly involved in secondary growths by this method (*see p. 709*). Implantation of free cells is believed to play a part in the spread of tumours in the renal pelvis, the ureter and the bladder. A papilloma of the bladder commonly gives rise to companion growths in this way, and a papilloma of the renal pelvis may lead to secondary masses in both the ureter and the bladder.

Another instance of implantation of free malignant cells is that which occurs at operation. It is especially apt to result from incision

of a tumour, as at biopsy, but it may occur whenever incomplete removal is carried out. There is no doubt that malignant cells are set free in a considerable proportion of incomplete operations, but actual implantation and growth is comparatively uncommon. "Recurrence" of carcinoma more often takes the form of a distant metastasis than of a secondary nodule at the site of operation.

## INCIDENCE OF TUMOURS

**Age Incidence** The varying age incidence of different tumours and of tumours in different regions is, of course, well recognized. A sarcoma usually arises in adolescence or in early adult life, carcinomata at a later age, though to this generalization there are many exceptions. The tendency to carcinoma becomes evident after the age of forty years and increases with advancing years, it is greatest in old age, but owing to the lower figures of total population in later decades most cases of cancer occur before the age of sixty years. Tumours in different sites show astonishing age variations: adrenal neurocytoma occurs characteristically in infancy, cerebellar glioma in childhood, bone sarcoma between the ages of fifteen and twenty five years, post cricoid cancer in the thirties, cancer of the prostate in old age, and the list could be multiplied time and again. In many cases as in tumours of such organs as the breast, prostate and ovary, the reason is possibly to be found in the cycles of functional activity of the part, in other cases no explanation is yet apparent.

**Sex Incidence** There are some noteworthy features concerning the sex incidence of tumours. Cancer of the breast and uterus have, of course, no counterpart in males, and for the greater part are related to the sexual functions or malfunctions of these organs, but the sex incidence of tumours varies in other parts of the body not connected with reproduction. Such sex divergences are common in the upper alimentary tract. Post cricoid cancer is found in women—comparatively young women—in 90% of cases. Cancer of the lower part of the œsophagus occurs principally in middle aged or elderly men, as does cancer of the stomach. In some regions the sex incidence can be explained by the habits of one sex or the other, as in most occupational cancers, and in cancers of the oral cavity, which are sometimes associated with pipe-smoking and with syphilis, but in other regions no predisposing factors can be found.

There are some interesting statistical features in relation to cancer of the breast, the uterus and the ovary. Cancer of the neck of the uterus usually occurs in parous women, but, as Deelman and others have shown, it is little more common in multiparæ than uniparæ. It would seem that the first confinement alone is responsible for the susceptibility to malignant change, and there is much evidence to show that the most important of these factors are laceration of the cervix during delivery and resulting cervical catarrh.

Cancers of the breast and the ovary, on the other hand, are common in nulliparous women. Possibly this is because they depend on some malfunction arising from lack of full physiological stimuli.

**Racial Incidence** The racial incidence of cancer has not yet been investigated upon a statistical basis sufficiently complete for definite conclusions, but there is at least evidence that cancer is known throughout the world and is common in every race. From time to time cancer is attributed to the influence of civilization, to desertion of the "natural mode of life," and even to specific habits thought to be limited to civilized peoples but, in general, each of these views is without scientific corroboration.

Curious differences do exist, however, in the racial incidence of certain forms of cancer. This has been most clearly established for Holland and Great Britain. It is found that in Holland the incidence of cancer of the breast is much lower than in Great Britain, but as though to compensate for this the Dutch women are more liable to growths in the alimentary tract. Statisticians are at a loss to account for these divergences in the absence of such factors as variations in diagnostic efficiency or differences in methods of compilation. As Greenwood points out, it will be interesting to note if similar differences obtain in various nationals living under comparable conditions in such a country as the United States of America.

### ALLEGED INCREASE OF CANCER

It is undisputed that in most countries during the past half century there has been a great increase in the recorded number of deaths from cancer, but in spite of this there is no complete proof that cancer has increased. There are obvious fallacies in drawing conclusions from the simple death rate, and of these the most important is that which arises from the ageing of the population due to improvements in public health and in the treatment of other diseases. The general population contains a far larger proportion of persons over forty years of age than it did a few decades ago, and the frequency of cancer is correspondingly greater.

In addition, there have been great improvements in the diagnosis and the recognition of cancer. Radiography, cystoscopy, and other diagnostic methods together with a ready recourse to exploratory operation have revealed many unsuspected new growths, and routine microscopic examination has shown that many apparently simple lesions *e.g.*, in the prostate or ovary, are actually neoplastic.

If allowance is made for ageing of the population it is found that the greater part of the alleged increase of cancer is referable to growths in inaccessible regions, whereas cancer of the skin, the mouth, and the neck of the uterus show little increase. For these and other reasons the balance of informed opinion inclines to the view that cancer in general has suffered no disproportionate increase. Exceptions, are, however, to be found in isolated types of cancer. Dunlop has shown that in Scotland there has been an absolute increase in the death rate from cancer of the breast, and since in death from this disease the cause can hardly fail to be recognized the incidence cannot be attributed to better diagnosis. Certain occupational cancers are undoubtedly on the increase, but this is in most cases clearly attributable to industrial



conditions (*see* p 71) It is almost certain that cancer of the lung is more common now than formerly, but the cause is unknown (*see* p 347)

## HEREDITY AND CANCER

This is one of the most controversial subjects in the whole field of cancer, and medical opinion on it is diverse and even contradictory. General statistics based on deaths from cancer are almost valueless, for quite apart from the inaccuracies of death certification the human stock is so mixed that satisfactory evidence for or against an hereditary basis would require full pedigrees, complete with medical histories, dating back for many generations

Most physicians of long experience must have met with families with apparently a strong disposition to cancer, and medical literature contains many such records One of the most famous is that described by Broca, in which sixteen members of a family of twenty six died from cancer of the breast, liver or uterus, and Warthin has related equally striking examples On the other hand, it is pointed out that even such remarkable figures may be explained on a basis of coincidence, for cancer is so common in man—in Great Britain it kills fully 10% of those who reach the age of thirty five—that any statistical evidence to be significant must deal with very large series of cases

In the experimental laboratory, however, these statistical fallacies may be eliminated, for with such a fertile, short lived, and conveniently small animal as the mouse it is possible to observe immense numbers of individuals whose pedigrees are known for many generations, and, moreover, by selective breeding the pedigrees may be so controlled as to eliminate many of the variables that confuse the issue in man. In this field the work of Maud Slye stands unparalleled in magnitude and result Many thousands of mice have been bred under strict conditions of mating, and every mouse has been subjected to detailed post mortem examination In the first 30,000 autopsies there were 4,000 primary spontaneous tumours Mammary carcinoma was by far the most common, but tumours of the lung and liver were not infrequent and there were many other types of simple and malignant growth

By selective breeding, Slye has produced remarkable results, for by the continued inbreeding of mice of cancer-bearing ancestry, she has produced strains of which every individual attaining maturity dies of cancer, and by inbreeding cancer free mice she has produced strains that appear completely immune to cancer She has, moreover, shown that the tendency to tumours of specific type or in specific organs is also hereditary. Some strains of mouse were liable to adenoma, others to carcinoma or to sarcoma, some were liable to tumours of the liver, others to tumours of the lung or of the breast From these and other experiments, Slye concluded that the tendency to cancer is hereditary, that cancer behaves as a unit character and that it is inherited as a Mendelian recessive

All Slye's conclusions are not accepted by other geneticists, particularly in regard to the Mendelian relationship—some regard it

as dominant, others as involving multiple factors—but there seems no doubt about the main thesis, the hereditary factor in cancer. It is not true to say that cancer itself is inheritable, but there is some hereditary disposition or diathesis which readily leads to cancer. Cockayne has recently reviewed Slye's work from this aspect. He concludes that the incidence of Slye's tumours depends upon some growth disorder such as adenomatosis, which is common in the three situations especially liable to cancer, namely, the lung, liver and breast. In the first two structures this factor probably behaves as a Mendelian recessive, in the last as a dominant. Cockayne also cites interesting examples in man of cancers dependent upon similar hereditary predispositions. An outstanding example is cancer of the colon, which often shows a remarkable familial incidence. In some of these cases the cancer is related to the condition of polyposis of the colon, an hereditary disorder of cell growth which behaves as a Mendelian dominant. Another example is neurofibromatosis, a Mendelian dominant which sometimes leads to malignant change, and a third is the common pigmented mole, which may dispose to the formation of a malignant melanoma. Many more such hereditary predisposing factors will no doubt be defined by further studies in genetics.

### TRANSPLANTABLE TUMOURS IN ANIMALS

When Jensen in 1903 published the results of his work on the propagation of mouse tumours he set the corner stone for a vast edifice of experimental tumour research, the results of which cannot fail to be of immense value in the general attack on the cancer problem.

Jensen's mouse tumour was a carcinoma, which occurred spontaneously in an elderly white mouse. By following the technique of previous workers he was able to transplant the tumour into other mice, and since then it has been transferred by grafting to millions more mice in laboratories throughout the world. At first the tumour only "took" in a small percentage of experiments, and principally in mice of the same breed, German mice, London mice, and wild mice of any origin were more resistant. In the course of time, however, the tumour adapted itself to these new hosts and eventually grew equally well in any variety of mice.

Jensen's work stimulated great interest in the study of animal tumours. *Contrary to general belief at that time, it was found that cancer is not exclusively a human disease, but occurs widely in many vertebrates, and in amphibians, birds and fishes as well as mammals.* It is particularly common in mice, and since they are convenient animals for laboratory study their tumours have been investigated most thoroughly.

It was soon found that tumour propagation is quite different from the transmission of any other disease. A tumour can only be propagated (except in the case of certain chicken growths which may not be strictly comparable) by the inoculation of living tumour cells, and all kinds of cell free extract or culture are innocuous. Moreover, tumour propagation is mere grafting. The new tumour cells are derived from the original host only, and each later host merely acts as a sort of living

culture medium whose function is to supply nourishment. When a carcinoma is transplanted its epithelial cells, or a small proportion of them, survive and proliferate, and they exact from their new environment a stroma with supporting tissue and blood vessels. Only very rarely do the cells of the new host become in turn malignant.

One of the most striking facts that has emerged from these studies is that in spite of the wide zoological distribution of cancer, and in spite of the great similarity of many growths in different kinds of animal, the transmissibility of cancer has very strict limitations in regard to species. A mouse tumour cannot be propagated to rabbits, a human tumour never "takes" in the lower animals. It is true that heterologous transplants have succeeded in certain special situations, as in the brain of rats or of guinea pigs and in chicken embryos, but apart from these few instances tumours can only be grafted in very closely related species. Another remarkable feature is the way in which a tumour runs true to type throughout its whole course. An adeno carcinoma remains an adeno carcinoma, and the very appearance of the cells may remain unchanged, as in the tumour described by Cramer, in which for fifteen years the cells retained their special property of storing glycogen. These are almost unsurmountable obstacles to a simple parasitic theory of cancer, for they would seem to postulate a separate strain of organism for each type of growth, as well as separate strains for each animal species.

**Chicken Tumours.** In recent years many studies have been made on certain chicken tumours. The best known of these, chicken tumour No. 1, described by Peyton Rous in 1911, was a spindle-cell fibrosarcoma, but since then several other types, all of connective tissue origin, have been studied. The chief characteristic of most of them is that they may be transmitted from bird to bird by means of cell free extracts as well as by living cells. In this respect they differ fundamentally from all known mammalian tumours, and for this reason many pathologists will not class them as true tumours but rather as infective granulomata resulting from unknown ultramicroscopic organisms.

It has been shown recently, however, that chicken tumours produced by the injection of tar extracts, which are undoubtedly true neoplasms, are also transmissible by means of cell free filtrates. This would seem to indicate that filtrability is a chicken characteristic rather than a property possessed by the individual tumours, and it lends strong support to the view that experimental observations made upon chicken tumours may be applied to the problem of cancer in man.

## EXPERIMENTAL PRODUCTION OF CANCER

It has already been related how, early in this century, the attention of experimental workers was turned to transplantable tumours in animals. Cancer research took another forward step with the discovery by Fibiger in 1913 and by Yamagiwa and Ichikawa in 1915 that cancer could be produced experimentally in animals.

Fibiger's brilliant study took origin from the examination of a spontaneous gastric carcinoma in a rat. In microscopic sections of the tumour he discovered the remains of a nematode worm, which he

identified as a parasite found in certain varieties of Danish cockroach. Further investigation disclosed a source of infected cockroaches in a local sugar factory. Fibiger then fed a number of rats on a diet of the cockroaches, and examined the stomachs of the rats at various intervals afterwards. In a short time after the start of the experiment the gastric mucosa developed signs of inflammatory reaction, this was followed by papillomatous proliferation and later, sometimes within three months,

by actual cancer, which invaded adjacent tissues and gave rise to metastatic deposits. Nematodes could be found in the primary gastric tumour but not in the metastases a significant observation which indicates that once the gastric cells had acquired malignancy they continued to proliferate in virtue of their own intrinsic energy.

Fibiger's work naturally aroused great enthusiasm for the parasitic conception of cancer, but with isolated exceptions there has been no evidence that other parasites behave like that particular nematode, nor can that nematode produce cancer except in the rat.

Recently, Passey and Leese have repeated Fibiger's experiments but have failed to confirm his findings. According to these workers, Fibiger's results were due, in part at least, to the fact that the rats used in his experiments were kept on a diet very deficient in vitamins, a state which is well known to produce papillomatous proliferation in the lining membrane of the fore-stomach.

The next method of experimental cancer production, discovered by Yamagiwa and Ichikawa, was of a different nature. It consisted in subjecting the skin surface to prolonged and repeated application of coal tar. Rabbits were first used for



FIG. 20. Carcinoma of the colon associated with polyposis. The tumour is of annular type and has caused extreme stenosis of the bowel. There are several pedunculated polyps of typical appearance in the dilated bowel proximal to the tumour.

this purpose, and the tar was applied to the delicate skin on the dorsum of the ear. Later it was found that mice are much more susceptible,

and that other substances than coal tar, *e g*, paraffin and shale oils have similar effects

When mice are painted twice or thrice weekly they develop first a thickening of the epidermis with warty or papillomatous growths, and these are later followed by the formation of a carcinoma, which invades, ulcerates and produces metastases. In most cases the carcinoma appears after about six months, but occasionally in as short a time as three months or in some cases only after an interval of eighteen months. If the tarring is carried out less frequently the tumour takes longer to appear, and the percentage of successful results is smaller. It is interesting to note that the growth may appear long after tarring has been abandoned, and in rare cases it has followed, after many months, when only a single application of tar has been made. Physical injury to the tarred skin, such as may be obtained by scarification, shortens the period of induction.

However extensive the surface tarred, only a single carcinoma develops, and when this happens any neighbouring warty growths disappear. This phenomenon is sometimes seen in various forms of paraffin cancer in man, and it suggests that possibly the presence of the malignant tissue induces retrogressive changes in neighbouring simple tumours, or more active defensive processes in the surrounding connective tissues.

Many attempts have been made to isolate the actual carcinogenic substances present in coal tar, and this has recently been achieved by Kennaway, Cook, Hieger and their associates. It was found several years ago that the active substances are present in largest amount in high temperature distillates of coal tar, and later it was noted that such distillates possess a characteristic fluorescence spectrum. Synthetic substances with similar spectra were then tested by applying them to mice. Amongst the substances tested was the chemical compound 1 2 5 6 dibenzanthracene, which had been newly synthesized by a firm of manufacturing chemists, and this was found to be actively carcinogenic. During the last few years a number of products allied to dibenzanthracene have been obtained, both by synthesis and by extraction from coal tar (*see also* p 75).

## PRECANCEROUS STATES IN MAN

It is now recognized that in a certain proportion of cases malignant tumours in man arise upon a basis of some chronic lesion of a simple nature. From some long continued irritative process the tissues undergo prelude changes of a proliferative nature which eventually culminate in cancer. It is hardly an exaggeration to state that study of these precancerous states constitutes one of the most fruitful avenues for cancer research and one in which there is prospect of fresh advances.

It has long been known that certain tumours arise on the basis of *congenital and inherited abnormalities*. Malignant growths may take origin, for example, in ectopic testes, in pigmented warts, in neurofibromatosis and other congenital lesions, the intensely malignant glioma of the retina occurs as a familial disorder, whilst carcinoma of

the large intestine arises not infrequently upon the basis of an inherited lesion, polyposis coli

*Simple tumours* occasionally become malignant, *e.g.*, fibromyoma of the uterus, though the great majority of simple tumours are no more liable than are normal tissues.

Various forms of *chronic irritation* constitute the last and in some respects the most important group of the *precancerous* conditions occurring in man

Carcinoma arises as a result of innumerable forms of chronic irritation. Carcinoma of the skin commonly occurs on a basis of old ulcers, burns, lupus, and the like; carcinoma of the mouth

or the lip commonly follows leukoplakia, or hyperplasia resulting from irregular teeth or the use of a clay pipe; carcinoma of the penis occurs when there is irritation from smegma retained behind a tight foreskin—it is consequently almost unknown in Jews; carcinoma of the stomach may arise at the edge of an old ulcer; carcinoma of the gallbladder may follow gall-stones. Lastly there are the tumours known as *occupational cancers*, which will be described separately below.

The relationship of these forms of chronic irritation to cancer will be discussed on a later page. It is sufficient here to note their great diversity of character.



FIG. 21. Cancer of the gall bladder, presumably associated with chronic irritation by the gall stones. The tumour a scabrous carcinoma, has infiltrated the gall bladder wall and produced an hour-glass deformity.

(Department of Surgery, University of Edinburgh)

Some are physical agencies, others chemical, and others again result from infection or infestation. This diversity would, at first glance, seem to indicate that there is no specific activity involved, and it is generally believed that the irritants do not actually cause cancer, but merely prepare the tissues for its origin. It is noteworthy that malignancy rarely develops unless the irritant has been effective during a considerable time, or has been frequently repeated, and that it may develop several years after the cause of irritation has been removed. The general view is that the effect of the chronic irritation is to interfere with cell nutrition, perhaps as a result of lymph

stasis, and thus to render the cells more liable to undergo malignant proliferation.

### OCCUPATIONAL CANCERS

Owing principally to modern scientific and industrial developments the number of occupational cancers is now considerable, and there is little doubt that it will increase in the future. There are a few tumours in this class, however, that date from long before the industrial era. Chimney-sweeps' cancer of the scrotum, resulting from the prolonged action of coal-tar products present in soot, is one of these. Another is the khangri cancer so common in Kashmir. The khangri is an earthenware jar contained in a basket and filled with burning charcoal, which the Kashmiri carries for warmth under the clothes in close contact with the abdomen, and it frequently causes burns which heal with much cicatrization. The scars very often become the site of development of a carcinoma.

The irradiation cancer (*see p. 106*), which has taken its melancholy toll of so many of the pioneers of radiography, is a familiar example of



FIG. 22. Shale oil cancer. A squamous-cell carcinoma, in a man aged fifty-five years, who had worked in a paraffin refinery during twelve years. A warty dermatitis had been present for several years, and the carcinoma developed in one of the warts.

an occupational cancer, and there are too the carcinoma of paraffin refiners and mule spinners, the bladder tumours of aniline dye workers, the pulmonary tumours of certain cobalt miners, and several others less well known.

Occupational cancers vary greatly in frequency, incidence, and clinical course, but practically all have these features in common: (1) the growth arises in men exposed for a period of years to the particular carcinogenic agent; (2) in the great majority of cases the growth is preceded by some precancerous condition, such as various forms of dermatosis; (3) the growth may begin many years after the worker has changed his occupation; (4) growths occur only in a small proportion of exposed persons, depending presumably on some idiosyncrasy.

**Shale Oil Cancer.** This form of cancer, though rare, is of interest owing to its relation to a particular industry. The tumour is almost

limited to the West Lothian district of Scotland, where it affects those engaged in the refining of shale oil (paraffin). It is a carcinoma and occurs principally on those parts of the body exposed to prolonged contact with the oil, in half the cases it occurs on the scrotum, in 30% on the upper extremities, and in the remainder chiefly on the face. Usually the tumour appears in men who have served during ten to forty years in the refineries, and it is uncommon in those of shorter service. It often occurs many years after retirement from work.

Scott showed that in most cases it occurs in men actually engaged in the refining process, and consequently in regular contact with hot oil. The cancer develops on a papular eruption or on a wart associated with a dermatosis such as frequently affects these workers. In other cases, however, the tumour arises in labourers who are little exposed to the oil, and in them it is not preceded by an obvious dermatosis. Presumably in such cases there is an idiosyncrasy.

**Mule Spinners' Cancer.** This is another form of paraffin carcinoma. It occurred in the "mule" spinners of Lancashire cotton mills, and did not appear to be known in cotton spinning districts in other countries. The "mule" required constant lubrication, and much of the oil was sprayed on the machine, especially at about the hip level. The men were thinly clad on account of the high temperature at which mule-spinning was carried on, and their clothes became saturated with oil. The cancer affected the scrotum, neck and arms. It usually occurred in spinners of twenty to forty years' service, and was often preceded by wart formation.

It is interesting to note that mule-spinners' cancer showed a rapid increase in Lancashire during the early part of this century. This is believed to be related to the fact that the period 1850 to 1875 saw a gradual transition from the use of animal (non-carcinogenic) oils to mineral oils derived from shale or petroleum. Only after the latent period of forty to sixty years did the effect of this change become manifest—a disturbing observation when considered in regard to the possible effect, many decades hence, of the modern pervasion of other petrolates.

## THE ORIGIN OF TUMOURS

No problem in the whole of pathology has evoked such a plethora of writings that "darken counsel by words without knowledge," of explanations that do not explain, and of theories that are insufficiently comprehensive. Few subjects offer greater perplexity and confusion to the inquiring student, and few are more difficult to present within unavoidably narrow limitation of space.

To understand the principal theories held in regard to the origin of tumours, and to appreciate the significance of recent experimental findings we must consider some of the fundamental features of tumour growth. In particular we must examine the behaviour of the tumour cell and discover in what respects it differs from normal cells.

**The Biology of the Tumour Cell.** It is a characteristic of nearly all tumours that their cells resemble more or less closely the cells of the



tissue from which they are derived, and this similarity of appearance holds good for the primary growth and for any metastatic growths that may develop

In spite of this morphological resemblance, it has until recently been the general opinion that tumour cells must differ from normal cells in some fundamental respect, in virtue of which they are endowed with a limitless capacity for proliferation

Many attempts have been made to discover wherein this difference lies, and to demonstrate in tumour cells a peculiar feature either of internal structure or of metabolism. It was claimed, for example, that tumour cells differ from normal cells in the number of their chromosomes, and when this was shown to be erroneous it was suggested that they differ in the character and disposition of the chromosome constituents, the genes

On the chemical side, the work of Warburg has furnished many interesting observations. It has long been recognized that cells, like bacteria, may be aerobic or anaerobic. Aerobic cells require oxygen for their nutrition, and derive their energy from the combustion of carbohydrates to carbon dioxide and water, anaerobic cells can live in the absence of oxygen by the fermentation of carbohydrates to lactic acid (anaerobic glycolysis). Now Warburg has shown that whereas the great majority of normal cells require oxygen, malignant cells subsist principally by anaerobic glycolysis, even though oxygen be available. According to Warburg, this property is an essential characteristic of malignant cells, and enables them to proliferate in circumstances inhibitory to normal cell growth. Even in this respect, however, malignant cells only differ from normal cells in degree, not in kind, for it has been shown that certain normal cells, for example those of the retina, possess glycolytic faculties equal to those of malignant cells, and to a smaller extent many other normal cells are similarly endowed, especially when actively growing.

During recent years most authorities have come to believe that tumour cells do not, in fact, differ in any fundamental respect from normal cells, and that their capability for limitless growth is not due to a special biological property but rather to freedom from restraint.

Nicholson, in a series of valuable papers, has lent the full weight of his authority to the view of the fundamental similarity of normal and malignant cells. He points out that tumour cells do not differ in essentials of structure or of growth from the cells of normal tissues, and that many simple tumours approach very closely in appearance to developmental malformations. A continuous gradation may be recognized for example, from uniovular twins at the one extreme through parasitic foetuses, teratomata and mixed tumours to the most highly malignant neoplasms. In his opinion, tumour formation is simply the expression of one of the physiological potencies of every living cell.

It is often stated that tumour cells are peculiar in their property of unlimited proliferation. It has been shown, however, by tissue culture experiments that this property is possessed also by many normal cells, provided that they are suitably nourished. Carrel, for example has

succeeded in propagating normal fibroblasts upon artificial media for as long as twelve years, and other normal cells have been maintained in active proliferation for shorter periods

Thus an inborn propensity for limitless growth is a characteristic feature of many, if not all cells. Normally their growth is restricted and controlled, so that the cells proliferate only to the extent necessary to meet the needs of the organism as a whole. In tumours, on the other hand cell proliferation is unrestrained.

**Older Theories upon the Origin of Tumours** Upon the observation that cancer sometimes develops at the site of congenital abnormalities, Durante advanced the view, later to be supported by Cohnheim, that tumours do not arise in normally placed tissues but in aberrant "cell rests." It was postulated that in the course of foetal life certain groups of cells failed to develop normally but persisted as "rests," which either remained embedded in their proper environment or were misplaced in other parts of the body, and it was believed that these "rests" retained special powers of growth which enabled them, after long periods of latency, to proliferate and form tumours. It is well known that portions of the adrenal and parathyroid glands and of the pancreas were often so displaced and it was supposed that similar malformations occurred in relation to other organs and other tissues.

Ribbert accepted the general principles of Cohnheim's theory, but extended it to include also acquired epithelial displacements such as may occur from overgrowth and fibrosis around any chronic inflammatory process. In Ribbert's view, islets of epithelial cells cut off from their normal relationships became released from physiological control and thus attained autonomy.

These and collateral theories held the field for a long time, but it is now recognized that they fail to explain many of the known facts of cancer and are totally inadequate except perhaps for a small proportion of tumours. For cancer cannot arise in "cell rests," unless these be ubiquitous, Ribbert's theory cannot be applied to sarcoma. Moreover, it is very doubtful if such "rests" as are known to occur are any more liable to neoplastic change than normal tissues. The time honoured example is the development of hypernephroma in adrenal rests in the kidney, but even this is now unacceptable, for most histologists believe the hypernephroma is of renal not adrenal derivation.

**The Parasitic Theory of Cancer** Many attempts have been made to demonstrate an organism as the cause of cancer, and there are few types of organism that have not from time to time been incriminated, but with the exception of Fibiger's nematode and one or two other parasites known to be related to specific forms of tumours none has stood the test of confirmatory experiment and none has received general acceptance. Many alleged parasites are now regarded as cell inclusions of various sorts, and others are generally looked upon as contaminants.

The parasitic theory has obvious attractions, but there are almost insurmountable obstacles to its acceptance, and all experienced pathologists are agreed that it is not consistent with the known facts. The greatest difficulty is to account for the narrow species limitation and

at the same time the wide zoological distribution of cancer. If cancer is caused by a single universal parasite, why cannot the disease be propagated from one species to another?

To overcome this difficulty Gye has recently formulated an ingenious hypothesis, which invoked a second, specific factor as well as a universal parasite. Gye's work was carried out principally upon the Rous chicken tumour, a peculiar form of sarcoma which differs from all mammalian growths in being propagable from cluck to cluck by means of filtered, cell free extracts. By centrifuge and by other methods Gye was able to separate such extracts into two moieties, which were innocuous alone but potent when mixed. These portions he believed to contain respectively the parasite and the second factor. As a result of these and other experiments Gye came to the conclusion that the parasite is present in all tumours, and is of the nature of an ultra microscopic, filter passing virus. The second factor, which is thermo labile and usually known as the "chemical factor," is specific for each species and for each type of tumour.

Ingenious though the hypothesis is, it has not proved acceptable, and his experimental results at present lack confirmation.

**Recent Work on Carcinogenic Agents** During recent years, the most notable progress in cancer research has been upon the relationship of cancer to various forms of so called chronic irritation, and particularly upon the characteristics of various agents capable of producing cancer experimentally.

In a previous section (p. 67) attention has been directed to the number and variety of the diseases that may be regarded as pre cancerous. It has been shown that cancer occurs as a sequel to many chronic inflammatory processes (burns, ulcers, lupus, cholecystitis, etc.) or as a result of such diverse agencies as X rays, soot, various paraffin products, arsenates and aniline dyes. It has, moreover, been related how cancer can be produced experimentally in animals by certain parasites or by coal tar products and other chemical substances. Thus it is apparent that the precancerous lesions are of widely differing character, some physical in nature, others chemical, and others again resulting from chronic infection or infestation. In view of their diversity of character, it is difficult to suppose that these agencies initiate the process of cancer in virtue of any single common factor, and most authorities hold the view that they do not actually cause the malignant change but rather prepare the tissues for its development.

Experimental investigation of the carcinogenic constituents of coal tar has recently yielded information that may well prove to be of the utmost importance in regard to the origin of tumours. Ever since the early experiments of Yamagiwa and Ichikawa (*see* p. 67), attempts have been made to isolate the active substances present in the tar, and this has at last been achieved by Kennaway and his associates at the Cancer Hospital, London. The active substances have not only been isolated in a pure state, but have been prepared synthetically.

When the coal tar products were first investigated it was found that the carcinogenic activity was greatest in high temperature distillates of the tar. Later it was found that these active distillates differ from the

inactive fractions in possessing a characteristic fluorescence spectrum whose intensity varies more or less in proportion to the potency of the preparation. Attention was then directed to synthetic chemical substances known to exhibit a similar spectrum, and some of these also proved to have cancer producing properties.

The most remarkable feature is that these substances are all closely similar in chemical composition. They are hydrocarbons, and each has a molecule containing four or five carbon rings arranged in a condensed formation. The majority are related to 1,2-benzanthracene, a substance which itself has hardly any cancer producing activity. The most potent of them yet discovered are 1,2,5,6-benzanthracene and 1,2-benzpyrene.

Thus in this particular series of cancer producing agents, carcinogenesis appears to be linked up with a special type of molecular structure. It is interesting to note that a somewhat similar structure is found in several substances normally present in the body, for example,  $\alpha$ -estrin and sterols such as cholesterol and the bile salts, and possibly the male hormone and vitamin D. It has been suggested that these substances may, under the influence of chronic inflammatory processes, X-rays or other agencies, undergo alterations of molecular structure and assume carcinogenic properties.

The conversion of one of these normal body fluids into a carcinogenic substance has already been achieved. By *in vitro* experiments the bile acid deoxycholic acid has been converted into the intermediate product dehydronorcholene and then by dehydrogenation into methylcholanthrene, which is actively carcinogenic when applied to the skin of mice. On general chemical grounds, however, it is doubtful if such a process can take place within the human body.

From the foregoing, it will be seen that our knowledge of the agents responsible for tar cancer has extended rapidly within recent years. It would clearly be dangerous to apply the findings in one particular type of cancer to the origin of malignant disease as a whole, but, nevertheless, the success gained in this limited field warrants the belief that in time the solution of the greater problem will in turn be achieved.

## CLASSIFICATION OF TUMOURS

In the present state of our knowledge no classification of tumours is beyond criticism, nor is any likely to be so until the aetiology of tumour formation is more clearly understood.

Tumours may be classified in either of two principal ways: (1) on a histological basis, according to the type of cell or tissue of which the tumour is composed, and (2) on a histogenetic basis, according to the primitive cell layer from which the tissue is thought to be derived.

There are so many intermediate and mixed types of tumour, and so many tumours of unknown or disputed origin, that any classification has patent disadvantages. For the sake of simplicity the following arrangement will be adopted—

## (1) Non-malignant Tumours of Connective Tissue Origin.

*Fibroma**Xanthoma**Lipoma**Myxoma**Chondroma**Osteoma**Myoma**Glomangioma*

## (2) Malignant Tumours of Connective Tissue Origin.

*Sarcoma*

## (3) Non-malignant Epithelial Tumours.

*Papilloma**Adenoma*

## (4) Malignant Epithelial Tumours.

*Carcinoma*

## (5) Teratoma and other Mixed Tumours

## (6) Tumours Derived from Nerve Tissue

*Glioma**Neurinoma**Ganglioneuroma**Paraganglioma**Glomangioma**Argentaffinoma*

## (7) Tumours Derived from Endothelium

*Endothelioma**Hæmangioma**Lymphangioma*

## (8) Melanoma

## (9) Chorion Epithelioma

In addition to these, there are a number of rare, obscure or indeterminate tumours which in the light of our present knowledge defy accurate classification. Such tumours as the giant cell tumour of bone, chordoma, and odontoma belong to this group.

## FIBROMA

Simple fibrous tissue tumours are widely distributed and are very common. Many of them, although termed fibroma, are actually of a more complex nature. A fibroma in the breast, for example, generally contains glandular acini, and in the present state of our knowledge is more accurately termed fibro adenoma.

A fibroma may arise from any of the fibrous tissues of the body, such as fascial planes, intermuscular septa, and submucous layers or from the connective tissue stroma of such organs as the breast, kidney, and ovary. They are very liable to cystic degeneration.

The common tumours arising from nerve sheaths were formerly regarded as fibromata. They are now believed to be of neural origin and are classified as neurinoma (p 814).

A fibroma varies in structure and appearance, according to its

cellularity and rate of growth, and it is customary to recognize two principal forms, hard fibroma and soft fibroma. These do not represent distinct types, however, and intermediate varieties may occur. A *hard fibroma* is usually small and of slow growth. It is of tough consistency, and when cut across it imparts a creaking sensation like cartilage. The cut surface is of grey colour and is traversed by glistening bands of fibres. Microscopically, such a tumour is composed of fibrous tissue of adult type, irregularly arranged in broad columns which pass in all directions. Cells are comparatively scanty, and there is a considerable proportion of collagen, often in a state of hyaline degeneration. Sometimes the cells have a somewhat whorled arrangement. A *soft fibroma* tends to grow more rapidly and to attain somewhat larger size. Microscopically, it is more cellular and with scanty fibrillar material. Some soft fibromata are so cellular as to resemble sarcoma. A *recurring fibroma* takes an intermediate position between a simple growth and a sarcoma. At first it is of a simple type and grows slowly, but after operation recurs repeatedly as if locally malignant and eventually may assume sarcomatous characters. The "desmoid tumour" of the abdominal wall, the "recurring fibroid of Paget," is of this type (see p. 216).

**Keloid.** Under the title of *true keloid* (as distinct from the common keloid of Alibert) Addison described a rare disease of the skin and subcutaneous areolar tissues. This remarkable disease arises spontaneously and is indicated first by a small oval white opacity or morphea in the skin. A zone of redness surrounds the patch, which later exhibits yellow or brown mottling. Following the development of new fibrous tissue, the surrounding skin becomes hard and rigid and processes of scar tissue extend for a considerable distance in the subcutaneous tissue. Finally the affected part, frequently an extremity, becomes hide bound and the seat of contractures. The skin, which may be excoriated, is puckered and nodular with a yellowish pink colour, giving it a resemblance to an extensive imperfectly cicatrised burn. The disease is progressive during many years and may implicate large areas of the body and limbs, and be associated with great pain and irritation. This variety of keloid is probably identical with scleroderma.

The surgeon is more familiar with keloid as a condition of excessive overgrowth of a scar, which results in firm, irregular, claw like masses of fibrous tissue projecting above the surrounding skin. The lesions may be single or multiple. The common places of origin are the face, neck and ears, and the front of the thorax and abdomen.

The lesion may follow any kind of injury, and it occurs in the scars of burns, tuberculous sinuses, vaccination marks, and healed skin diseases, as well as in those of surgical wounds. Even insignificant injuries such as insect bites and pin pricks have been the starting point of the disease.

A decided predisposition to overgrowth of scar tissue and keloid exists in some subjects. Negroes exhibit this tendency more obviously than whites and it is stated to be pronounced in tuberculous subjects. Infection of the original wound is undoubtedly a common predisposing factor, and it is the only known one of any significance.

A recently developed keloid has the appearances of a redundant scar and has a shiny pink or reddish appearance. Its surface may be smooth, rough or furrowed, and in some sites such as the lobe of the ear, it may be pendulous. The margins of a keloid are not sharply defined and project irregularly into the subcutaneous tissues or even into the deep fascia and muscles.

Histologically, a keloid has the structure of a soft fibroma, and is composed of dense bundles of fibrous and hyaline connective tissue with well defined fibroblasts, which are disposed more or less parallel to the cutaneous surface. The periphery is more cellular than the centre and shows a round cell infiltration. There are no hair follicles, sweat glands, muscle fibres, or elastic tissue in the tumour, but newly formed blood and lymph vessels are present. The overlying epidermis is thin and is often devoid of papillae.

A keloid shows no tendency to disappear spontaneously, and it tends to recur, especially if removed during its active period of growth. Although it exhibits some of the characters of a malignant growth it never gives rise to metastases.

### XANTHOMA (Xanthelasma)

The term xanthoma is applied to a group of yellowish brown growths of the skin which present very diverse characters. The tumours are situated most commonly in the eyelids (*Xanthoma palpebrarum*), where they may be single or multiple. Less often they have a diffuse distribution throughout the cutaneous surfaces (*Xanthoma multiplex*). Rarely they have been observed in the pharynx, in the mediastinum, and in serous membranes such as tendon sheaths. Xanthoma sometimes occurs in association with diabetes (*Xanthoma diabeticorum*).

Histologically a xanthoma shows the characteristics of a benign connective tissue tumour localized to the corium. It is distinguished by the presence of numerous large rounded mononuclear cells, containing droplets of cholesterol esters and of orange yellow lipid material. In ordinary fixing agents these droplets are dissolved, and therefore leave vacuoles in the cytoplasm, hence the name "foam cells."

The origin of the characteristic "foam cells" is uncertain. Some trace them to fixed cells of the connective tissue or to the endothelium of lymph or blood vessels, others to wandering phagocytic cells. Ewing



FIG 23 Subcutaneous xanthoma  $\times 120$ . There are numerous large foamy, lipid-containing cells in the dermis and subcutaneous tissue.

(Royal College of Physicians of Edinburgh)

believed that many xanthomatous tumours of the skin are due to lipoid infiltration of cutaneous neurofibromas.

*Xanthoma palpebrarum* may affect either the upper or the lower eyelid and is often bilateral. The tumours, which are of slow growth, are usually flat and bean shaped and have a canary yellow or muddy brown colour. They are soft and are situated in the subepidermal layer of the skin.

*Xanthoma multiplex* occurs particularly in young subjects and is sometimes congenital. The lesions, which resemble pigmented fibrous tumours, are specially common in the neighbourhood of joints as well as on the face and trunk. They may be arranged in groups with a symmetrical distribution.

A number of the subjects of this form of xanthoma subsequently develop diabetes and in many of the recorded cases jaundice has been present.

Probably the most common predisposing cause of xanthomatous tumours is hypercholesterolemia, which has been shown to be present in some cases. This view is supported by the observation that the intracellular lipoid is a compound ester of cholesterol and fat, such as is normally present in such organs as the ovary and suprarenal gland, and, in certain conditions of disease, in the gall bladder, spleen and blood vessels. Such a metabolic predisposition would explain the occurrence of xanthoma in diabetes and in jaundice, states often characterized by an increase of the cholesterol content of the blood.

It is interesting to note that xanthomatous tumours may be produced experimentally in rabbits fed with large amounts of cholesterol and subsequently submitted to aseptic traumatization of the subcutaneous tissues. The cholesterol is deposited from the blood and subsequently undergoes phagocytosis by large mononuclear cells, and these cells assume the characteristic 'foamy' appearance.

Under the general heading Xanthomatosis we may include certain other diseases characterized by the accumulation of lipoid laden cells in various organs or tissues. Amongst these are *Gaucher's disease*, a chronic familial affection occurring in children, especially females, and characterized by great enlargement of the spleen due to the accumulation of cerebrosides within its reticulo-endothelial cells, the *Atemann Pick disease*, a rapidly fatal disease of Jewish infants characterized by enlargement of the spleen and liver due to the accumulation of phosphatide such as lecithin, and the *Schüller Christian disease*, in which xanthomatous tumours occur in the bones especially of the skull.

## LIPOMA

A lipoma is the commonest tumour of the subcutaneous tissue and may occur in almost any part of the body, although it shows a predilection for the regions of the shoulder, back, and buttocks. Less commonly a lipoma grows in an intermuscular space, under the periosteum, or in the submucous or subserous layers of the alimentary canal. It is a soft, well demarcated, movable swelling which is very often lobulated. The overlying skin is often loosely attached at one or more points to



the capsule of the tumour and is therefore obviously dimpled, or becomes so on pressure

A lipoma appears in adult life and usually grows very slowly, and having attained a certain size remains stationary, but occasionally growth is rapid and the tumour may attain a very large size. When situated in the back it may, by gravity, gradually alter its position. In the region of the buttocks, the groin, and the perineum it often becomes pedunculated.

A lipoma is usually composed of round fairly firm, yellow masses or lobules. It is surrounded by a fibrous capsule which is firmly connected with the surrounding tissues, but only loosely connected with the tumour. Protrusions of the capsule pass between the lobules of the tumour and constitute its fibrous trabeculae.

A lipoma is essentially a benign tumour, and sarcomatous change



FIG. 24. Lipoma removed from the thigh of a man aged sixty three years. The lobulated character of the tumour is clearly seen.

is exceedingly rare, although primary tumours of the nature of *liposarcoma* have been described. They occur mainly in the retroperitoneal tissues or subcutaneously in the shoulder region. They invade diffusely, and may be painful. In most cases they are of low malignancy and responsive to irradiation therapy.

Some lipomata have an abundant and dense fibrous stroma and may be appropriately called *fibro-lipoma*, others are excessively vascular—*haemangio lipoma*, and others again present myxomatous, cartilaginous, and xanthomatous elements. Occasionally a lipoma of long duration undergoes degenerative changes such as liquefaction and calcification.

*Multiple lipomata* are not uncommon. The individual tumours in this condition are seldom large, but they may be very numerous and scattered over the whole of the body surface, and as many as 2,000 have been present in one subject. In some instances they may be symmetrically disposed, as in the forearm, where they are sometimes painful and associated with motor, sensory and trophic disturbances.

A *diffuse lipoma* (pseudo-lipoma) usually occurs in the subcutaneous tissues and intermuscular tissues of the neck of men, where it gives rise to a bulky collar like swelling. It is not a true tumour but a localized overgrowth of the fat of this region, which in some cases can be attributed to chronic alcoholism. Somewhat similar overgrowths may occur in the hips and thighs, especially in women. From their tendency to give rise to severe pain these overgrowths have been given the name *adiposus dolorosa*.

Excessive deposits of fat may occur in the supraclavicular region in myxœdema, and in the genital area in hypopituitarism.

### MYXOMA

A myxoma is a soft tumour composed of translucent jelly like tissue resembling the delicate mesenchyme of the umbilical cord (Wharton's jelly). Microscopically, it consists of branching stellate cells set in a clear mucoid matrix. Such tumours arise usually in relation to tendons, periosteum or joints, or occasionally in the heart. They are usually small, encapsuled growths, but sometimes attain large size. A pure myxoma is an extremely rare growth, but tissue of the character just described is of frequent occurrence in other tumours, such as nasal polypi, a chondroma, a neurofibroma or sarcoma. In such circumstances it is to be regarded as resulting from degenerative changes (mucoid or myxomatous degeneration).

### CHONDROMA AND OSTEOMA

These tumours are considered fully in the chapter on "Diseases of Bones," to which reference may be made (*see p. 157*).

### MYOMA

Muscle tumours may be composed of either plain or striped muscle fibres. A *leiomyoma*, or tumour of plain muscle fibres, is by far the commonest. The site most frequently affected is the uterus, and the uterine myoma is one of the commonest of tumours in the whole body (*see p. 684*). Less often a leiomyoma arises from the muscle fibres of the œsophagus, the stomach (*see p. 480*) the bladder, or ovary. Rare examples have been found in the skin, and are believed to arise from the *muscles arrectores pilorum*. A leiomyoma is usually a benign encapsuled growth, but occasionally it is subject to sarcomatous change. It is described fully on p. 684.

A *rhabdomyoma* is a tumour composed of well differentiated striated muscle fibres. It is exceedingly rare but has been encountered most often in young subjects especially in the soft palate and the tongue, and less often in the bladder, the uterus the vagina and the œsophagus. When the tumour arises from a mucous surface its appearance is characteristic, showing a lobulated coarsely polypoid structure with broad clubbed processes. It is locally destructive and may metastasize by the lymph or the blood stream. In structure a rhabdomyoma

appears superficially to be well differentiated, but a closer examination reveals groups of very anaplastic or primitive round and spindle cells to which it probably owes its very malignant tendencies

Some examples of rhabdomyoma are composed entirely of undifferentiated cells resembling morphologically and in staining characters primitive muscle cells—*myoblasts*. Such tumours have a homogeneous cellular pattern, and though the cells lack the mature cellular structure of a typical rhabdomyoma, the tendency to malignancy is much less. This type of rhabdomyoma has been styled myoblastoma by Cappel and Montgomery

Striated muscle of varying degree of maturity is an occasional constituent of teratoid tumours, *e g*, of the kidney, testis, and ovary

## SARCOMA

Malignant tumours derived from connective tissues are generally of extreme malignancy. They grow rapidly, invade surrounding tissues, disseminate to distant parts of the body at an early stage, and quickly lead to a fatal issue. Within the bounds of this general statement there are, however, many variations in behaviour. Some sarcomata, notably those arising in bone, are almost invariably fatal, but others are less aggressive, while a few only achieve recognizably malignant characters after a prolonged existence

A sarcoma is much less common than a carcinoma, and differs from it in several important attributes. Sarcoma may occur at any age, though some forms notably bone sarcoma are most common in early life. A sarcoma generally grows rapidly and forms a large soft tumour. With few exceptions it tends to disseminate early by the blood stream. This method of dissemination is no doubt chiefly due to the copious blood supply of a sarcoma and to the delicate nature of its vessel walls which are readily invaded by tumour cells

A sarcoma may arise from any type of connective tissue, and it consequently has a wide distribution in the body. It originates most often in relation to bone, or from the periosteum, cartilage, fascia, and intermuscular septa or in the subcutaneous tissues, less often it occurs in submucous tissues or in the stroma of internal organs

In a certain proportion of cases a sarcoma arises in a previously benign tumour, *e g*, uterine myoma, fibroma, chondroma. Sometimes it arises on a basis of some generalized growth disorder, *e g*, neurofibromatosis, osteitis deformans, osteitis fibrosa. Occasionally trauma appears to determine the onset of the growth

The cells of a sarcoma may remain fairly well differentiated and continue to reproduce, to some extent, the structure of the parent tissue, or they may revert completely to the primitive state. Thus a sarcoma arising in fibrous tissue may continue to produce more or less well formed collagen fibrils or may be entirely cellular. When the nature of the parent tissue is recognizable, such terms as fibro sarcoma, chondro sarcoma, osteo sarcoma, lipo sarcoma, and myo sarcoma may be employed. Tumours composed of undifferentiated cells are usually

contains collagen fibrils (*fibrosarcoma*) Occasionally a sarcoma is composed of such well differentiated cells and matrix that the distinction from a simple fibroma, or even from granulation tissue, may be made only with great difficulty

Other sarcomata are composed principally of small round cells Most of these are *lymphosarcomata*, tumours which arise in lymphoid tissue, and differ in many respects from other sarcomata (*see p 254*) Other sarcomata are described, but recent researches show that they are extremely rare, and that most tumours formerly so classified are lymphosarcomata

Many other varieties of sarcoma are recognized, according to special features of the cells or of the intercellular matrix—for example, chondro sarcoma, osteo sarcoma, myxo sarcoma, and lipo sarcoma These are described on other pages

## PAPILLOMA

A papilloma is a simple epithelial tumour which projects from an epithelial surface Although essentially an epithelial structure, it always includes connective tissue elements, which form a core, simple or branching, containing lymph and blood vessels It appears as though



FIG 26 Papilloma of the skin  
(Laboratory of Royal College of Physicians of Edinburgh.)

the growing epithelium can evoke a connective tissue framework to support and nourish it

A papilloma may arise from any epithelial surface, and the following types may be recognized (1) from the epidermis, (2) from mucous membranes (3) from duct walls, (4) in certain cysts and cystic tumours

Cutaneous papillomata are common in childhood and are usually multiple, the skin of the hands and fingers being frequently affected The growths are the result of a virus infection, and after a varying period disappear spontaneously Venereal papillomata, which affect the skin of the genital organs, are also of infective nature As Cathcart suggested in 1897, they are not due to gonococci, and there is evidence that they arise from some form of filter passing organism

A papilloma arising from epidermis or from any squamous cell membrane, such as the mucous membranes of the tongue, mouth,

larynx, œsophagus or vagina, is composed of a core of connective tissue surmounted by squamous epithelium. The epithelium may resemble the normal tissue but often presents variations, such as undue thickening of the rete Malpighii or of the stratum corneum.

Villous papilloma of the bladder and renal pelvis forms a special type of tumour. It reproduces the transitional epithelium of the urinary passages, and consists of connective tissue cores surmounted by a few layers of rounded or oval cells. It is composed of innumerable filamentous processes of great delicacy, and, since the stroma is vascular, it is very apt to cause profuse hæmaturia. It frequently recurs after operation, and may eventually prove malignant (see also p. 619).

A papilloma is common in the large intestine, and may occur in the stomach, small intestine or gall-bladder. It is composed of columnar cells on connective tissue cores and is usually pedunculated. Since the columnar cells tend to reproduce to some extent the glandular structure of the alimentary tract the papilloma is somewhat complex, and often is of the nature of an adenoma rather than a papilloma. In the colon these growths are apt to become malignant. It is interesting to note that in Egypt schistosomiasis frequently gives rise to multiple outgrowths in the bladder and rectum indistinguishable from true papilloma and equally liable to malignant change.

Papillomata arising from the ducts of glands occur with great frequency in the breast, in association with so-called chronic mastitis. They are described in more detail in the chapter on diseases of the breast. Similar papillomata are very common in the biliary tract of rabbits where they form multiple columnar-cell outgrowths from the walls of the intrahepatic bile ducts. The peculiar interest of this condition is that it occurs only in rabbits affected by coccidiosis, and that the oocysts of the parasite may be seen closely related to the tumours—a striking example of new growths due to parasites.

Papillomata arising in cyst walls are seen most frequently in cysts in the breast and ovary but may occur in other organs. The cysts referred to are not simple distension cysts, but depend primarily upon proliferation of the epithelial lining cells and it is consequently not surprising that in some the proliferation takes the form of intracystic projections in place of simple enlargement of the cyst. In some cases the presence of intracystic papillomata is an indication of early or potential malignancy—the papillomata are the first evidence of the ability of the cells to grow atypically. Thus in the ovary a papilliferous cyst is considerably more liable to malignancy than a multilocular cyst.

## ADENOMA

An adenoma is a simple tumour derived from glandular epithelium. Like a papilloma, it also contains connective tissue which serves to support and nourish the epithelial elements, varies greatly in amount, character and vascularity. When the stroma preponderates, as in many breast tumours the term *fibro-adenoma* may be used.

An adenoma reproduces with some degree of exactness the glandular structure of the parent tissue and indeed some adenomata, e.g., in

the breast or thyroid, can be distinguished only with difficulty from the normal glands. Moreover, the cells of the tumour may function, adenoma of the thyroid gland contains colloid material and may produce thyroxin, adenoma in the gastro intestinal tract secretes mucus. Since the tumours possess no properly formed ducts the secretion may remain impounded in the acini and form cysts, *e.g.*, in the breast, thyroid, and ovary. The epithelial wall of such a cyst may continue to proliferate and may give rise to intracystic projections of the character of papillomata. These are particularly common in an ovarian cystic adenoma. An adenoma lying close to a free surface tends to project therefrom, and may eventually become pedunculated, and in the gastro intestinal tract may subsequently initiate intussusception.

Adenomata do not appear to bear the same relation to chronic irritation as do papillomata, but, on the other hand, in a number of cases seem to be associated with some developmental disturbance, in that they possibly originate in glandular cells dislocated from their normal environment. Foetal adenoma of the thyroid gland appears to arise in this way, as do adenomata of the colon, which, furthermore, have a familial incidence.

An adenoma may arise from any glandular tissue in the body. It occurs most often in the breast, ovary, thyroid, and glands of the alimentary tract. More detailed description of individual types is found in the chapters devoted to these regions.

## CARCINOMA

This is the commonest form of malignant new growth, and is the form usually indicated by the term "cancer." Its frequency may be judged from the fact that more than 10% of those who reach the age of thirty five years eventually die of cancer.

Carcinoma differs from sarcoma in several respects, which have already been alluded to. (1) it occurs generally later in life. The incidence rises steeply in the fifth and sixth decades, and most cases occur at this time of life. Often the age incidence of cancer coincides with the period of functional senescence of the affected tissue, *e.g.*, the breast, uterus prostate. (2) Carcinoma usually grows less rapidly than sarcoma, and does not disseminate at such an early stage. There are exceptions to this general rule, however, notably the case of melanotic carcinoma, which often grows rapidly and disseminates early. (3) Carcinoma tends to spread first and principally by the lymph vascular system and only later invades the blood stream. (4) Microscopically a carcinoma is composed of cells of epithelial type, which tend to be grouped in masses or columns. The individual cells lie closely apposed, with little or no intercellular matrix. Occasionally, however, carcinoma cells growing rapidly become spindle shaped like the cells of a sarcoma and may lie singly in the stroma.

The amount and character of the stroma varies greatly in different tumours and in different parts of the same tumour. When in large amount and composed of tough fibrous tissue it gives the tumour a

hard (scirrhous) character and since the fibrous tissue shrinks the tumour is usually of small size. Scirrhous tumours are common in the breast, stomach and colon. In the alimentary canal the fibrous contraction may give rise to a ring stricture.

Occasionally, as in the "leather bottle stomach," excessive stroma appears to strangle and isolate the epithelial cells, which are then identified with difficulty. None the less, however, scirrhous tumours are no less malignant than other types, and often tend to infiltrate widely.

A carcinoma with scanty stroma is commonly larger and softer than scirrhous growths, and sometimes it merits such a title as encephaloid or medullary. Often a tumour is scirrhous in some parts and encephaloid in others. The metastases from a scirrhous tumour

are often of encephaloid type.

Three principal types of carcinoma may be recognized: (1) squamous-cell carcinoma, (2) basal cell carcinoma, (3) glandular carcinoma.

(1) **Squamous-cell Carcinoma** (*squamous epithelioma*). Tumours of this class may arise from the skin and its appendages or from the stratified squamous membranes of the upper air and food passages and the vagina. They may also arise by a process of metaplasia from other epithelia, e.g., from the transitional



FIG. 2.—Squamous-cell carcinoma (epithelioma) of the skin. On the right there are numerous rounded masses of malignant cells, some with cell nests. Note the hyperplasia of the epidermis close to the tumour.

(Department of Surgery, University of Edinburgh.)

epithelium of the urinary tract and the columnar-cell membranes of the gall bladder, uterine neck, etc.

Squamous-cell cancer may develop spontaneously in previously normal skin, but it is particularly liable to occur at parts that have, during a long period, been subjected to some form of irritation. The irritation may have been mechanical, thermal, chemical, or bacterial, or have resulted from various combinations of these agencies. It is therefore common for cancer to follow eczema, warts, or hyperkeratosis of the skin, and in such cases the site and character of the skin lesions, and the cancer that follows them, are usually determined by occupations that involve exposure to chemical or other irritants. Thus, in irradiation

cancer, the backs of the fingers, from neglect of protection, are usually affected; in tar and pitch workers, chimney sweeps, and mule spinners the scrotum is affected. In addition to the above predisposing or pre-cancerous factors may be mentioned chronic ulcers, cutaneous horns, the scars of burns and of lupus, and psoriasis patches. In lupus carcinoma exposure to X rays often appears to have been the determining factor, and in psoriasis prolonged application of arsenic often seems to be responsible.

There are two types of squamous-cell cancer (1) the papillary, and (2) the ulcerating. Intermediate forms are common.

*The papillary type* takes the form of a wart or nodule of variable size with a broad base. Ulceration tends to occur at the surface of the growth, and as a result dry crusts are formed on it. Beneath the crusts the tumour is pink in appearance, and is indurated.

*The ulcerating type* causes an irregular breach of the surface of the skin. The edge of the ulcer is firm and indurated and its base is hard and granular. There may be considerable penetration into the subcutaneous tissues. On the face the ulcer may originate in a small red pimple, which grows rapidly and breaks down to form a slightly raised crateriform ulcer.



FIG. 23 Squamous epithelioma of nostril

Microscopically, a squamous cell carcinoma is composed of masses of angular cells in solid clumps with bud-like processes extending irregularly into the subcutaneous tissues or the cells may be arranged in whorls in which the characteristic cells surround cornified epithelium (*epithelial pearls* or *cell nests*). The latter appearance indicates a high degree of cellular differentiation, and consequently a relatively low grade of malignancy. In some growths fibrils or spinous processes connect the cells, hence the name *acanthoma* or *prickle cell tumour*.

A squamous cell cancer of the skin spreads by direct infiltration of adjacent tissues. The rate of growth varies in different cases and according to the age of the subject, and the character of the tissues which surround it. Generally, warty growths tend to be less aggressive than the ulcerous. After a variable period the growth usually metastasizes to the regional lymph glands, which become enlarged. Visceral metastases are uncommon.

At some sites, especially the nasopharynx and tonsil, squamous cell



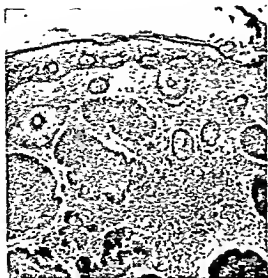


FIG. 29. Basal-cell carcinoma (rodent ulcer) of the skin.  $\times 75$ . The tumour is composed of large circumscribed masses of epithelial cells, the outer layers of which are of typical basal-cell character. The tumour is covered by a thin layer of skin.

carcinoma may show marked anaplasia. The stroma is composed of cells of sarcomatous character (usually lymphosarcoma), so that the tumour has blended the features of carcinoma and sarcoma—*carcinosarcoma or lympho-epithelioma*.

**Squamous-cell Cancers at Special Sites.** *Cancer of the penis* starts on or just behind the glans, less often on the inner aspect of the prepuce, and very rarely in the skin of the body of the penis. In many instances the growth begins in a wart, an old scar, or a patch of

leucoplakia. Phimosis and chronic balanitis frequently precede cancer at this site, and must be regarded as predisposing factors, because the occurrence of cancer is extremely rare in the circumcised. Occasionally a glandular type of cancer occurs and probably originates in the glands at the corona or frenum.

The growth is usually of a flat papillary or cauliflower type and may reach considerable size before ulceration occurs. It is pinkish-red in colour and it is firm and hard. At first it remains confined to the glans penis, but later perforates the fibrous envelope of the corpora cavernosa and infiltrates the erectile tissue. The urethra is seldom invaded. Metastases occur in the inguinal lymph glands on one or both sides.

A carcinoma of the penis



FIG. 30. Basal cell carcinoma (rodent ulcer) of the lower eyelid at an early stage of growth.

is usually concealed behind a tight prepuce, therefore its presence may only be suggested by the club like enlargement of the organ or by the offensive discharge or bleeding to which it gives rise

*Lupus cancer* may develop at the margin of the ulcers of lupus, or in the thin scars which follow healing. Many years may elapse after healing before the appearance of the growth

A lupus carcinoma is usually of an exuberant or cauliflower type and grows slowly, and like other cancers which develop in scar tissue it has little tendency to spread to the lymph glands, as the intervening channels are obliterated by fibrosis. In advanced stages the subjacent bones may be extensively involved by direct spread of the tumour (Fig 88)

Lupus carcinoma frequently develops at an earlier age than other forms of squamous cell cancer of the skin. Its development often appears to be precipitated by irradiation by X rays or radium

*Cancer in chronic ulcers* of the skin occurs rarely. The growth usually appears at the edge of the ulcer. It takes the form of a hard, granular excavation which spreads very slowly in the surrounding skin and subcutaneous tissues, and may finally penetrate the adjacent bones. Spread to the regional



FIG 31 Basal cell carcinoma rodent ulcer. High power photograph of the edge of the tumour  $\times 450$ . The tumour consists of masses of epithelial cells bounded by a single palisade row somewhat resembling the basal layer of the epidermis

(Laboratory of Royal College of Physicians of Edinburgh)

lymph glands is a late occurrence because the lymph vessels have usually been obliterated by long standing lymphangitis

Chronic leg ulcers, though very common lesions, are only rarely the seat of carcinoma

(2) **Basal-cell Carcinoma (RODENT ULCER)** This is an ulcerating tumour arising from the basal cells of the skin or from cells of similar derivation in hair follicles and sweat glands. It occupies a position intermediate between simple and malignant growths for though locally invasive and destructive it extends very slowly and does not metastasize. It rarely occurs before middle age, and males are affected more often than females. In the great majority of cases the tumour arises in the skin of the face, especially in close proximity to the medial or lateral palpebral commissure or in the naso labial fold less often in the frontal and temporal regions of the scalp. Tumours of similar character



FIG 32 Basal cell carcinoma involving the eyelid and cheek in an advanced state

arise occasionally in the skin of other parts of the body, and sometimes in the squamous-cell mucous membranes, such as the tongue, pharynx and oesophagus.

At its inception the tumour lies deep to the epidermis, and at this stage may appear as a firm red papule or as a flat, slightly raised plaque. At an early stage, or rarely after a considerable period, the superficial epidermis gives way, and the growth then takes the form of an ulcer. Rarely two or three such ulcers may coexist.

The appearance of a rodent ulcer is characteristic. The surface is red and granular, and when small is usually covered by a dry crust or scab. The edge may be

smooth, regular, and cleanly cut, but often is slightly rolled or beaded. It is not raised and thickened to the same extent as in a squamous cell carcinoma. Around the edge and at the base of the ulcer there is generally a moderate amount of induration. Occasionally at one edge the erosion may be arrested temporarily, and a thin pellicle of young epidermis may grow in from the margin. Such a healing process is always very limited in extent and temporary, however, and in untreated cases it never prevails.

Spread of a basal cell carcinoma is slow, but progressive. At first the tumour extends mainly at the expense of the sur-



FIG 33 A columnar cell adenocarcinoma of the breast  $\times 100$ . The acini vary in size and shape. They are lined by columnar cells, which in places are several layers deep. The supporting stroma is scanty and the blood vessels are thin walled.

rounding skin and subcutaneous tissue, but later it involves deeper structures which it invades erodes and destroys. The regional lymph glands may enlarge as a result of infection but metastases do not occur. In a few well authenticated cases malignant change has supervened. Such a change may follow inadequate irradiation therapy.

Microscopically, a basal cell carcinoma is composed of epithelial cells disposed either in large, somewhat rounded masses, or in narrow columns and processes. Between and around the masses of cells is a stroma of richly cellular fibrous tissue, which is often infiltrated with lymphocytes and other inflammatory cells as a result of superadded infection. At first the tumour is covered by a thin layer of epidermis, and it is sometimes possible to trace a connexion between the deep surface of this layer and the epithelial cells of the tumour. Later when the growth is ulcerated, the thinned out epidermis is only visible at the edge.

The epithelial cells at the periphery of the cell masses are of low columnar shape and are arranged in a single palisade layer, somewhat like the basal layer of the epidermis. The remainder of the cells, deep to this layer, are smaller, and polyhedral in shape.

A basal cell carcinoma contains no cell nests and few prickly cells an important feature which distinguishes it from squamous cell carcinoma. Usually the cell masses are solid but occasionally there is an irregular adenomatous appearance and degenerative changes may lead to the formation of small cystic spaces.

The origin of a basal cell carcinoma is generally believed to be from the basal cells of the epidermis but the adenomatous arrangement sometimes present has suggested that in some cases the epithelium of sweat glands or hair follicles provides a starting point. In view of the close morphogenetic relationship of these structures such a belief is reasonable.

### (3) Glandular Carcinoma

This term is generally held to include tumours arising from columnar or cubical cells of mucous membranes and ducts as well as from the glandular elements themselves.

Glandular carcinoma occurs in many parts of the body. It is commonest in the breast, stomach and large intestine, but may occur



FIG 34 Spheroidal-cell carcinoma of the breast

in other parts of the alimentary tract, for example, the gall bladder, pancreas, liver, and in such organs as the ovary, uterus, prostate, kidney, adrenal gland and thyroid.

The cells of a glandular carcinoma may differentiate to the extent of reproducing, to greater or less degree, the acini of the gland, or they may form solid masses with no glandular architecture. Thus two types may be recognized: (1) adenocarcinoma, in which there is some tendency to the formation of acini; and (2) spheroidal cell carcinoma, in which no glandular structure is recognizable.

*Adenocarcinoma* is commonest in the alimentary tract, but may occur in the other organs mentioned above. The acini are but imperfect

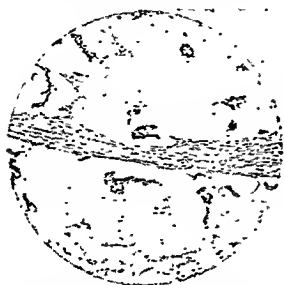


FIG. 35. Mucoid cancer of the colon. Scanty epithelial cells lie in small groups separated by large quantities of mucoid material.

reproductions of the glands from which they are derived, and they show many deviations from the normal. They vary greatly in size, and since they possess no ducts for evacuation of their content they become distended with retained secretions, epithelial debris, etc. The lining membrane is no longer formed of a single layer of cells, but may be many cells deep, and having no basement membrane the cells penetrate the subjacent stroma. The individual cells have the characteristics of

malignancy and are large and deeply stained, and often show mitotic figures.

In some glandular tumours, e.g., those of the ovary, the thyroid, and occasionally the breast and kidney, the cells have a papillary arrangement—*papillary adenocarcinoma*.

In *spheroidal-cell carcinoma* the cells are arranged in solid, round, circumscribed masses with no glandular formation. This type of tumour occurs most often in the breast, less frequently in other glands. By mutual pressure the cells may assume polygonal shape.

*Mucoid (Colloid) Carcinoma*. This type of growth occurs most often in those regions where mucin-forming cells are normally present in large numbers, e.g., in the stomach, colon, gall bladder, but they may occur elsewhere, for example, in the breast. The epithelial cells produce large quantities of mucin, which first distends the cells and then escapes into the intervening matrix. Eventually the greater part

of the tumour may be replaced by mucin. The tumour is usually massive, with a characteristic semi translucent appearance, and of soft, jelly-like consistency. Microscopically, the malignant cells are scanty, and of degenerate appearance, and the great bulk of the tumour is composed of clear gelatinous material.

Mucoid carcinoma is generally believed to result from degenerative changes which may occur in any form of glandular carcinoma, but in certain features it differs entirely from ordinary forms of degeneration. Mucin is the specific secretion of the cells, and it occurs in metastases as well as in the primary tumour. Moreover, it has been shown in animals that the potentiality for this change may be transmitted through many generations of tumour. It is often stated that mucoid degeneration is an index of a relatively low grade of malignancy, but there are many exceptions to this rule. In the breast, it is true, most mucoid carcinomata grow slowly and metastasize late, but occasionally breast tumours of this type are extremely invasive, and mucoid carcinoma of stomach, gall bladder and bowel tend to grow rapidly and spread widely.

### MIXED TUMOURS

On previous pages it has been shown that practically all epithelial tumours, innocent or malignant, possess a stroma of connective tissue. The term "mixed tumour," however, refers only to those growths in which both types of tissue are integral parts of the tumour, and participate equally in its neoplastic character.

It is believed that all the cells of a mixed tumour have a common ancestry from a single cell of embryonic type, which has retained its primitive capacity for producing different kinds of tissue. It is obvious that the more primitive the cell the greater its potentialities, and so there may be (1) multipotent cells capable of producing various kinds of mesodermic tissue (cartilage, muscle, bone, fibrous tissue, etc.) with or without glandular elements, and (2) totipotent cells capable of producing any or all types of cell or tissue.

Tumours arising from multipotent cells occur most often in the kidney and the testis and ovary, and are considered in detail in the chapters devoted to those organs. A tumour derived from totipotent cells is generally known as *teratoma*, less often an *embryoma*.

**Teratoma.** This term should be restricted to tumours derived from totipotent cells, and should not be used to include mixed tumours of less complicated type, such as occur in the kidney or salivary glands.

There are two distinct classes of *teratoma*: (1) those recognizable at birth, and usually situated close to the surface of the body; (2) those appearing after birth or in adult life, and usually affecting internal organs.

A *teratoma* recognizable at birth represents incomplete uniovular twins. It is usually situated in the sacro coccygeal region, and projects on the surface of the *autosome*. Sometimes it takes the form of complete limbs or of parasitic twins in various degrees of perfection. The most extreme examples are the fully formed conjoined twins,

which may be regarded as mutual teratomata. In other cases a congenital teratoma is a shapeless mass containing in irregular confusion a great variety of tissues or portions of organs. Such masses are commonest in the sacral region but may occur in the region of the upper jaw, and the term *epignathus* may then be applied.

A teratoma developing after birth or in adult life is found most often in the ovary or the testis but it may occur in other situations for example the brain, mediastinum, or the retroperitoneal tissues (*extragenital teratoma*). It has been suggested that it arises from parthenogenetic development of germ cells, but it seems more probable that the origin is from blastomeres or from undifferentiated germ cells totipotential cells derived from the early embryo, which have been sequestered or remained inactive during development.

The tumour may be either solid or cystic, and it may contain tissues derived from all three embryonic layers. Stratified squamous epithelium, sebaceous glands, hair follicles and enamel organs lie irregularly disposed among masses of cartilage, bone, and muscle, and various gland-like structures lined by columnar epithelium are also present. Even Langhans cells and the syncytium of chorionic epithelium occur and occasionally they may constitute the greater part of the tumour, even when it is situated in the testis.

Ovarian teratoma is often cystic. It is sometimes known as ovarian dermoid, for it may resemble an inclusion dermoid cyst. There is a large cavity containing hair and sebaceous matter and projecting from the wall of the cavity may be a hard plaque covered with skin and often containing teeth. An ovarian teratoma differs from inclusion dermoids in possessing tissues derived from all the three primary layers and in addition to skin derivatives it contains muscle, cartilage, glandular structures, and even thyroid tissue and nerve cells.

Teratomata are not necessarily malignant tumours, and some of them, especially those situated in the ovary, remain stationary for many years or only enlarge by the distension of their cystic spaces. Others however, notably teratomata in the testis, are usually very malignant. The malignant change may affect one or several of the constituent tissues, though not always in equal degree.

### TUMOURS DERIVED FROM NERVE TISSUE

Tumours of nerve tissue may arise in the central nervous system, in peripheral nerves, in the trunks and ganglia of the autonomic system, and in various tissues such as the adrenal medulla, which are closely allied developmentally and functionally.

In the brain and spinal cord the common tumours arise from the supporting fabric (neuroglia) and only very rarely from the nerve cells. *Gliomata* present many different types according to the degree of differentiation of the predominating cells and they may grow slowly or with extreme rapidity. They are considered fully on p. 274. True tumours of the peripheral nerves are extremely rare. It is possible that the acoustic neuroma is a true tumour of nerve tissue, and its characteristics are considered in detail on p. 280. The tumours commonly

called neurofibroma or false neuroma are not derived from nerve tissue but from the investing sheaths of nerves. The so-called amputation neuroma or stump neuroma is merely hyperplasia of the cut nerve fibres (*see* p. 320).

Tumours of autonomic nerves form an interesting group of new growths, which have been more clearly recognized in recent years. Formerly they were confused with sarcoma, to which they bear great resemblance. They are the commonest malignant tumours in infants. Tumours of this class arise from the ganglia of the autonomic system and they are most commonly situated in the retroperitoneal tissue

and in the mediastinum. They arise not from neuroglia but from the embryonic nerve cells (sympathicoblasts). Most often the cells are of immature type, hardly recognizable as nerve cells, and the terms *sympathicoblastoma* or *neuroblastoma* may then be applied. Such tumours commonly occur in infants or young children, and grow rapidly and metastasize widely. Less commonly the cells are fully differentiated and resemble the ganglion cells of the autonomic system. Such tumours, *ganglioneuroma*, take a

benign course. Either neuroblastoma or ganglioneuroma may also arise from the adrenal medulla, a tissue closely related in origin and function to the autonomic nervous system (*see* p. 604). Tumours similar to a neuroblastoma may arise in the retina from the primitive cells of the central nervous system. They are usually of familial incidence and arise in infancy or early childhood.

In recent years certain tumours have been described which are believed to take origin in chromaffin tissues in various parts of the body. The most outstanding examples of such tumours, which have been termed *paraganglioma*, are the tumour of the carotid glomus, and the chromaffinoma of the adrenal medulla.



FIG. 36. Ganglioneuroma  $\times 300$ . The tumour was situated in the retroperitoneal tissue. Note the characteristic ganglion cells, unipolar and bipolar. Nerve fibres also are present, and small cells of neurolemma type.

(Laboratory of Royal College of Physicians of Edinburgh)

### TUMOURS DERIVED FROM ENDOTHELIUM

Until the last decade endothelial tumours were generally believed to be of common occurrence, but with stricter pathological criteria



in the recognition of endothelial cells it is now clear that this was a mistaken view. Endothelium forms the lining membrane of blood vessels and lymph vessels, and the pleura, pericardium and peritoneum. But with the exception of hæmangioma and lymphangioma, primary tumours of these tissues are extremely rare. Tumours of the pleura or peritoneum, for example, are almost invariably secondary to some growth, perhaps of very small size, of the underlying viscera or in distant situations. And the so called dural endothelioma is now believed to arise from the arachnoid mater, which is not considered to be an endothelial structure.

Tumours of the endothelium of blood vessels and lymph vessels are described on pp 233 and 254 respectively.

## MELANOMA

### Physiology of Pigmentation

The dark races owe the colour of their skin to the pigment melanin, and in them it affords protection for the underlying structures against the powerful rays of the sun. The pigment is most abundant in the basal layers of the epidermis, but it may be present as high as the stratum granulosum or even the stratum corneum. In the fair races pigmentation is present only in the skin of the nipple, the axilla and the ano genital region, but in the foetus the basal layer of the skin in other parts of the body is pigmented and becomes depigmented soon after birth. The capacity for pigmentation, however, is retained in adult life, and under the action of intense sunlight or ultra violet irradiation the skin becomes bronzed or freckled, and it is then noted that the deeper layers of the epidermis acquire melanin pigment, and that the stratum corneum becomes deeper. As the sunburn or freckling disappears the cells slowly give up their pigment. In the pigmented basal cells melanin is distributed in the form of brown or black granules of fairly uniform size which are aggregated around the upper pole of the cell nucleus.

In the basal layer there are, in addition, pigmented cells of a *dendritic* type, and these are present in greatest number when a stimulus to pigment formation, such as sunlight, X rays, or ultra violet radiation, is applied to the skin. As transition forms between this type of cell and the ordinary basal cells can be traced, it is believed that they are derived from normal basal cells, and that the assumption of dendritic processes is evidence of an active phase of pigment formation. Their origin from basal cells is also substantiated by their specific staining qualities (*see below*).

Pigmented cells of somewhat similar appearance are also found constantly in the dermis, especially around the blood vessels. The origin and function of these cells has given rise to considerable discussion. From their peculiar staining affinities it is believed that they arise from the connective tissue of the corium, and that they are not specifically concerned with the elaboration of melanin, but with its disposal, and for this reason they have been termed *chromatophores*. The pigment in

the cells is in the form of irregular globules, and it is believed that they acquire it from the epidermis

Apart from the skin, melanin occurs in the pigmented structures of the eye (retina, chorioid, iris, and ciliary body) In the central nervous system it is found in the substantia nigra and, in varying amounts, in the meninges

Melanin is the only pigment normally found in the skin of man It is elaborated by cells of the epidermis, and the cells with this property are known as *melanoblasts* Melanin contains no iron in its complex molecule, and hæmoglobin plays no part in its formation, sulphur is present, probably only as an impurity The ultimate source of melanin, like adrenalin, is tyrosin In lower animals, melanin is formed in the cells of the epidermis directly from tyrosin, through the action of a ferment or oxydase—*tyrosinase* In higher animals, however, the process is more complicated, and before reaching the pigment forming cells, tyrosin is converted into a colourless chromogenic substance known as dihydroxyphenylalanine (DOPA) This substance, on reaching the pigment forming cells, is converted to melanin by a specific intracellular ferment, called by Bloch *dopa oxydase*

The conversion of *dopa* into melanin in the melanoblasts may be demonstrated *in vitro* Bloch demonstrated that sections of skin soaked in a solution of *dopa* showed deposition of melanin in only those strata in which pigment formation normally occurs (*viz.*, the deeper layers of the epidermis), and this behaviour of the skin is known as the *dopa reaction* It is likely that the *dopa reaction* resembles very closely, or is identical with, the normal process of melanogenesis The reaction is only evidenced in those cells in which *dopa oxydase* is present, *i.e.*, in cells that are melanoblastic, actively or potentially, and the results suggest that melanin formation is almost entirely a function of tissues derived from ectoderm, and of the skin in particular

When *dopa* is applied to frozen sections of human skin the basal layers become blackened, due to the deposition of granules of melanin in the cytoplasm of the cells, and the intensity of pigment production coincides with the existing amount of pigment present in the skin examined The dendritic cells of the epidermis, referred to above, also show a positive *dopa reaction*, but the pigmented branched cells of the



FIG 37 Symmetrical melanoma of front of chest

(Museum of Royal College of Surgeons of Edinburgh)

corium (melanophores) are dopa negative suggesting that the melanophores are not of epidermal origin, and that they do not produce, but merely carry pigment.

In some pathological states there may be generalized or localized diminution of pigmentation of the skin, in others there may be an increase. In albinism, there is total absence of melanin from the skin, hair and eye, and the dopa reaction of these structures is negative. In vitiligo, the reaction is negative in the depigmented areas of the skin and is strongly positive in the adjacent zones of hyperpigmentation. In Addison's disease, brown pigmentation may be uniformly distributed throughout the skin surfaces of the body, or it may be relatively excessive in certain areas. It is believed that the precursor of adrenalin is identical with dopa, and that when the suprarenal glands are diseased they are unable to utilize their normal quota of the mother substance, therefore, it is surmised, the pigmentation of the skin is evidence of a compensatory action of the melanoblasts to utilize the excess of chromogenic agent. Accordingly the dopa reaction of the skin in Addison's disease is weak, because the dopa oxydase has already been utilized in the formation of melanin pigment.

### TYPES OF MELANOMA

A melanotic tumour or melanoma arises most often in the skin, rarely in the eye or in other parts of the body. It is usually present at birth and the term *nevus* (Latin *naevus*—a birthmark or blemish) may be applied to it, less commonly, it becomes obvious about puberty, or in adult life. There is evidence that a melanoma may result from trauma.

A congenital melanoma is represented in simplest form by a flat or slightly raised pigmented spot or macule. When more pronounced it may take the form of a warty, pedunculated, or hairy mole. Sometimes tumours of this class are very numerous and may be disposed in groups or in irregular lines (systematized and linear melanoma). Occasionally they form large diffuse patches, sometimes distri-



FIG. 38. Secondly pigmented melanoma of acanthotic and keratoid types. The pigmentation is confined to the epidermis and there are no epithelial cells in the corium.  
(Laboratory of Royal College of Physicians, Edinburgh.)

buted symmetrically on the trunk or limbs (giant melanoma). The bathing trunk pattern of diffuse pigmentation, sometimes found in association with generalized neurofibromatosis, is an exaggerated example of this variety.

Mast melanomata are simple tumours and remain so throughout life, but some, after remaining unchanged during many years, may enlarge and show signs of malignancy, and occasionally a melanoma is malignant from its onset. According to these modes of behaviour, the melanomata may be described conveniently under three headings (1) benign melanoma, (2) malignant melanoma arising in benign growths, (3) malignant melanoma arising *de novo*.

### (1) Benign Melanoma

Two main types of benign melanoma may be recognized (a) the "hard" or secondarily pigmented melanoma, (b) the "soft" or *nævus cell* melanoma. The two types can be distinguished only by histological examination, and the essential difference is that in the former type, the secondarily pigmented melanoma the pigmented cells lie entirely within the epidermis, whereas in the latter type some of the characteristic cells of the tumour, the so called *nævus cells*, lie deep to the epidermis in the corium.

"Hard" or Secondarily Pigmented Melanoma. This should be regarded as a warty growth which is pigmented, and in which the pigment appears to play an entirely subordinate role. It is peduncu-



FIG. 39. Benign *nævus-cell* melanoma. Note the groups of *nævus cells* regularly arranged in the upper part of the corium and the thickening of the overlying epidermis.

(Laboratory of Royal College of Physicians of Edinburgh.)

lated or sessile and may be discrete or aggregated. It may arise from the stratum corneum of the epidermis (*keratoid type*), or from the prickle cell layer (*acanthotic type*). These tumours differ from other forms of melanoma in that they seldom become malignant, and that, when they do, they give rise to typical squamous cell carcinoma, not to malignant melanoma.

Soft or "*Nævus-cell*" Melanoma. This tumour consists of aggregations of cells in the deeper layers of the epidermis as well as in the corium. The cells in the epidermis are usually elliptical and non-fibrillated, and are arranged in groups or cell nests, which cause expansion of the rete processes of the epidermis.

The cells in the corium are round, mostly non-pigmented, and arranged in regular groups or columns. These cells are known as *nævus cells* and they are characteristic of this type of tumour. The *nævus cells* are separated from one another, and from the epidermis, by a variable amount of connective tissue. The cells are of spherical shape, with scanty cytoplasm and a round or oval nucleus which has a definite

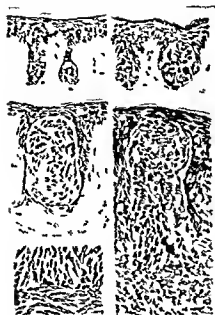


FIG 40 Stages of evolution of a malignant melanoma.

(Laboratory of Royal College of Physicians of Edinburgh)

and arise from the endothelium of lymph and blood channels (Von Recklinghausen) or from undifferentiated connective tissue cells (Ribbert) (2) they are epidermal in origin and arise from specific cells—melanoblasts (Unna Dawson), and (3) they are related in their origin to the terminal nerve fibres of the skin (Soldau Masson Ewing)

Dawson from elaborate histological studies adduced strong evidence to uphold the epidermal origin of the naevus cell. He was able from a large series of sections to trace the processes by which they arose from localized areas of pigmented cells in the deeper layers of the

nucleolus and a clear chromatin network. They show a faintly positive dopa reaction and are therefore presumed to be capable of melanin formation. At the periphery of the columns of naevus cells and in the adjacent tissue there are a few pigmented granular cells of branching or rounded shape which are believed to be ordinary phagocytic cells containing pigment (melanophores). In a few cases of naevus-cell melanoma the histological changes are confined to the epidermis.

The problems of melanoma and the exact origin of the naevus cell are very complex and do not admit of dogmatic answers. The histological interpretations are difficult and uncertain. The various views may be classified thus: (1) the naevus cells are mesodermal in origin



FIG 41 Simple melanoma showing malignant transformation. Note the melanoblasts spraying from the rete processes and also the irregularity of the naevus cells in the upper corium.

(Laboratory of Royal College of Physicians of Edinburgh)

epidermis. He stated that, "the process could be traced from the localized areas of pigmentation of the basal cells, through a series of cell transformations occurring in those cells, to the formation of intra epidermal cell nests", and that "in the intra epidermal formations the epithelial cell, having lost its intercellular fibrils, becomes detached and actively proliferative, assumes a spindle or star shaped form till finally the cell group or its component cells break through the transition zone between epidermis and corium, leaving the superficial layers to heal up while they themselves migrate and settle in the upper corium where they undergo regressive processes, and become the atrophic cells of the naevus. They arise, however, as melanoblasts and remain potential melanoblasts though they become depigmented and give up their pigment to chromatophores on the periphery of the cell groups".

The researches of Masson, which have been amplified by Ewing afford equally strong evidence that the naevus cell is a derivative of specialized cells found in association with the sensory nerve ends in the corium or in the epidermis or in both. Their views have now gained general support, they certainly offer a simple explanation of the pigment changes found in neuro fibromatosis—itsself a disease affecting specially neuro-ecto dermal structures—suggesting the active participation of epithelium in a melanoma may be referred to the growth of specialized cells belonging to the nerve end apparatus.

## (2) Malignant Melanoma (Arising in a Benign Growth)

The presence of melanin in the cells of a simple melanoma appears to lead to a state of instability and a tendency to malignancy. It is sometimes observed that a benign melanoma that has remained unchanged during many years unexpectedly shows enlargement increased vascularity and finally malignancy.

The change may occur spontaneously, or it may be initiated by trauma. The signs of malignant change may appear gradually, or they may occur with great suddenness manifest by



FIG 4\* Malignant melanoma of the sole of the foot

local infiltration, enlargement of lymph glands, or the appearance of metastases. In other cases evidence of malignant change is evidenced by local recurrence after removal of an apparently simple growth. It is important to realize that increase in size may be an inconspicuous feature of malignant transformation, for, in some sites, such as the nail bed and the eyeball the tumour may be extremely small, and may have escaped detection, and in such cases, widespread metastases often occur without apparent enlargement of the primary growth.

Transition to malignancy in a benign melanoma appears to be a dual process and is caused by proliferation of the quiescent naevus cells and the multiplication of new cells derived from the surface epithelium, especially the rete processes. Histologically, these changes are marked by the appearance of larger protoplasmic forms of "naevus cells," which often show two nuclei. These cells tend to become free from the pre-existing cell groups and to form isolated masses. Coincident with these changes the rete processes in the epidermis increase in number over a variable distance and become broad and club-shaped, due to proliferation of the cells within them. At different parts the rete processes rupture, and pale protoplasmic cells penetrate into the corium, where they proliferate and give rise to stellate or spindle-shaped forms with a variable degree of pigment (see Fig. 40).

### (3) Malignant Melanoma (*Arising de novo*)

A malignant melanoma may occur at almost any point on the surface of the body, but common sites are the forehead, the neck, the abdominal wall, and a nail fold. The nail fold or bed is the commonest of all. In some sites the primary tumour remains small although metastases may be numerous, in others the tumour may grow rapidly to a large size and may ulcerate.

In general, a malignant melanoma may be regarded as the most aggressive of all tumours. It has pronounced infiltrating characters and therefore spreads widely by direct extension.

In addition it tends to invade the lymph vessels, giving rise to metastases in the regional lymph glands. The tumour cells may actually grow in the lymph vessels and give rise to multiple and/or massive secondary growths in their course. The secondary deposits in the lymph glands are frequently more deeply pigmented than the primary growth.



FIG. 43. Small ocular melanoma with multiple secondary nodules in the liver. Some of the nodules are non-pigmented.

(Department of Pathology, University of Edinburgh.)

In many cases a malignant melanoma metastasizes by the blood stream and gives rise to multiple secondary growths in the lungs, brain, liver, kidney, and skin. Metastases may be so numerous and widespread that the condition is known as *generalized melanosis*. In a few cases the secondary tumours are non-pigmented or only pigmented in patches. A tendency to spontaneous retrogression of the metastases has been observed in a few instances. In a few instances of generalized melanosis careful search has failed to reveal the primary focus. In some instances a metastatic tumour does not come to light until many years after the removal of the primary growth.

Histologically, the most striking feature of the malignant melanomata is the diversity of their structure, and according to the form and configuration of the cells they may be divided into three main groups: (1) melano carcinoma, in which cells of epithelial character are arranged in alveoli, (2) the melano sarcoma, composed of spindle cells, and (3) melano endothelioma. Transitional forms may occur or there may be striking variations within the same tumour.

Ocular melanoma arises from those parts of the eye which normally contain pigment. It occurs most often in the conjunctiva, the choroid, and the pigmented layers of the retina, and more rarely in the iris and ciliary body. Usually it is highly malignant.

Melanoma of the bulbar conjunctiva does not differ greatly from one in the skin. It forms a flat diffuse growth which often overles part of the cornea. It tends to recur after operation, and removal of the eye may be necessary for its eradication.

Intra-ocular melanomata are of two varieties, (a) circumscribed, and (b) diffuse.

(a) *The circumscribed tumour* is often lenticular in shape. It usually occurs in the choroid, from which it may spread to the subretinal space, and then assumes a mushroom shape. The sclera resists invasion for a considerable time, and, as a result, there is great disorganization of the interior of the eye. After the sclera is in filtrated extension to the perforating arteries or the optic nerve occurs. Metastases, usually in the liver and lungs, may develop while the primary growth is exceedingly small. Local recurrence after removal of the eyeball is not common.

Histologically, this type of tumour shows great structural polymorphism, not only in the different tumours but in the same tumour. The commonest appearance is that of a pigmented spindle or round-cell sarcoma. Pigmentation is irregular and may only be present in groups of cells or the pigment may be in clumps between cells.

(b) *The diffuse tumour* is characterized by longer duration of growth and by a greater tendency to spread by the perivascular lymph channels. The cells in this type are polygonal or spindle-shaped and vary considerably in their pigmentation.

Dawson claimed that all the ocular melanomata were of epithelial origin, and that the histogenesis was the same as in melanotic tumours of the skin. He based his claims on the essential structural similarity of the skin and the conjunctiva, and on the neuroectodermal origin of the normal pigmented cells of the retina and choroid.



## IRRADIATION OF TUMOURS

Increasing use of X rays and radium in the treatment of tumours makes it imperative for the surgeon to be familiar with the pathological results which may follow excessive dosage by these types of irradiation.

In general, the effects of X-rays and of the gamma rays of radium are similar, except that X-rays, being necessarily applied externally, have their maximum effect upon the integument, whereas radium if introduced below the surface acts principally upon the tissues immediately around it. The disturbance may be constitutional or local, and in either case may be acute or chronic. Acute effects are seen in patients as a result of excessive exposure to the rays, whereas chronic effects occur usually in radiologists, the result of prolonged and repeated irradiation.

**Constitutional Effects of Irradiation.** Acute constitutional disturbance is manifest within a few hours or a few days of the time of irradiation. When mild, it is characterized by headache, malaise, anorexia etc. when severe it may lead to vomiting, diarrhoea, prostration and death. The toxæmia responsible for these manifestations has been attributed variously to acidosis, alkalosis, destruction of white blood cells, disintegration of leucithin, derangement of the colloidal equilibrium, and alterations in chloride distribution in the body fluids. Chronic constitutional effects are characterized principally by degenerative changes in the blood forming tissues. Secondary anaemia develops, with leucopenia and a relative lymphocytosis. Sometimes leukaemia or aplastic anaemia supervenes.

**Local Effects of Irradiation.** The local effects of irradiation vary greatly depending, on the one hand, upon the intensity and duration of the exposure and, on the other, upon the radiosensitivity of the tissues. The radiosensitivity is a variable factor, for it depends not only upon the type of cells but also upon their state of activity at the time of irradiation. In general, the most sensitive of normal cells are the germ cells, the lymphocytes, and the highly specialized parenchymatous cells of viscera, especially the liver, spleen, thyroid gland and bone marrow. All cells are most sensitive during growth and multiplication. These aspects form the basis for therapy in certain non-malignant diseases. Thus treatment by X-ray or radium is valuable in certain forms of hyperthyroidism and in some disorders of the spleen and bone marrow. It also affords relief in certain inflammatory conditions, for example, dermatitis, diverticulitis and rheumatoid arthritis, although its mode of action in these diseases is not understood.

The local action of irradiation has been investigated more thoroughly in the skin than elsewhere. When the skin is exposed to a single "overdose" of irradiation it may exhibit any degree of damage from mild erythema to a deep burn. These effects are usually not manifest until several days after exposure. Irradiation burns are characterized by failure to heal during long periods, for the irradiation effects an obliterative endarteritis with fibrosis of the surrounding tissues, and consequently the sloughs are slow in separating and the processes of repair are delayed.

If insufficient to produce such acute effects irradiation may result in changes that become manifest only after a period of weeks or months. The cells of the hair follicles and sweat glands are often destroyed, and consequently the hair subsequently falls out and the skin becomes dry and shiny. Often the skin becomes deeply pigmented.

Repeated irradiation of the skin may give rise to chronic dermatitis, and this may lead to an "irradiation carcinoma" (X ray carcinoma). Such effects are almost limited to radiologists, and, as a consequence of the former practice of holding the fluorescent screen in the unprotected hands they are situated most often on the dorsal aspect of the fingers. It is interesting to note that an irradiation burn such as results from simple overdosage shows no special liability to the development of malignant disease. The chronic skin lesions are due essentially to endarteritis obliterans, perivascular fibrosis, and oedema of the cutis vera, as well as to secondary changes in the epidermis. The nails become corrugated and brittle, and eventually separate from the matrix. The skin becomes red, shiny and atrophic, and later pale, dry and thickened. Sometimes ulcers develop, which tend to penetrate deeply and to remain unhealed during long periods. Later, multiple papules and warty nodules appear, the harbingers of cancer.

Irradiation cancer arises usually on the basis of one of the warty nodules. It occurs as a late manifestation, and may develop many years after the final exposure to irradiation. In some cases two or more independent carcinomata arise. The growth has the microscopic characters of a squamous cell carcinoma, but since the tissue is fibrous and the lymph vessels are extensively obliterated the growth spreads slowly and metastasizes late.

**Effects of Irradiation on Tumours** In accordance with the general concept that the radiosensitivity of cells varies according to their activity, tumour cells are generally more susceptible to irradiation than normal cells, and the cells of malignant tumours are generally more susceptible than those of simple tumours.

If a radium needle be implanted in a tumour, its effects vary in different parts of the tumour inversely as the square of the distance. Immediately around the needle the tissue, both cells and stroma, rapidly undergoes necrosis, and eventually forms sloughs, small or large according to the dosage. In the zone peripheral to this area the cells undergo a form of coagulation necrosis and are destroyed, but the stroma, being less vegetative, survives, and consequently no gross sloughing occurs. In a zone more peripheral, the rays destroy only a proportion of the tumour cells, more particularly those in mitotic division at the time. Other cells not destroyed are believed to be subjected to inhibitory influences which have the effect of restraining their growth.

In irradiation therapy the aim is to effect maximum tumour destruction with minimum damage to the normal tissues. This object is achieved by accurate estimation of suitable dosage and careful distribution of the needles so as to obtain a uniform field. It is generally believed that successful treatment is enhanced by the use of relatively small amounts of radium over a long period which ensures that during



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## CHAPTER VIII

### DISEASES OF BONES

THE problems of osteogenesis, normal and pathological, remain the subject of unabated controversy. Bone has been described as a connective tissue impregnated with lime salts, but, though true enough, this simple statement gives no indication of the complicated structure of bone, so beautifully adapted and adaptable to bodily needs, nor of its manifold functions in relation to metabolism and its responses to hormonal influences. These anatomical and physiological considerations have such a close bearing upon the pathology of bone diseases as to necessitate a detailed account of them.

#### ANATOMY OF BONE

For illustration a typical long bone will be considered. Such a bone consists of a shaft or *diaphysis* and of two extremities or *epiphyses*. During the period of growth the diaphysis is separated from the epiphyses by plates of hyaline cartilage, the *epiphyseal cartilages*. Some bones possess, in addition, secondary epiphyses or *apophyses*, which are separated from the diaphysis or the primary epiphyses by plates of cartilage.

From the pathological standpoint the most important part of a bone is the *metaphysis*, the region of cancellous bone immediately on the diaphyseal side of the epiphyseal cartilage. This is the region from which all lengthwise growth of bone proceeds, it is the most vascular region of the bone, and it is the region most liable to injury. For these reasons it is especially apt to be involved in trauma or in infective disease in childhood or adolescence, and it is especially affected by any interference with the normal processes of calcification and ossification during those periods. It is also the region most subject to tumour formation.

**Blood Supply.** The distribution of blood vessels in bones is of importance in determining the sites affected by disease.

In a typical long bone the sources of blood supply may be classified as follows: (1) The nutrient artery, (2) periosteal arteries, (3) metaphyseal (juxta-epiphyseal) and epiphyseal arteries.

(1) *The nutrient artery* is a vessel of considerable size, which supplies the major portion of the bone. It enters the bone usually at its middle third, in a direction obliquely away from the larger metaphysis. Inside the bone the artery divides into two principal groups of vessels, which are directed in the long axis of the bone towards either end of the shaft. They terminate at the metaphysis by anastomosing with other vessels to be described below.

(2) *The periosteal arteries* are fine twigs which supply the superficial layers of the cortex of all parts of the bone. They are large and abundant in childhood, scanty and small in old age.

(3) *The metaphysial (juxta epiphysial) and the epiphysial arteries* are fine vessels derived from the arterial plexus (the *circulus vasculosus* of Hunter) which form a network encircling the bone in close relation to the joint capsule. These vessels penetrate the periosteum and cortex to reach the metaphysis and epiphysis respectively, and they terminate by anastomosing with the terminal branches of the main nutrient artery. Thus it will be seen that the metaphysis, the region of maximum bone growth, is supplied by three sets of blood vessels: (1) terminal branches derived from the main nutrient artery, (2) metaphysial arteries, (3) epiphysial arteries that have penetrated the epiphysial cartilage. These anastomosing vessels at the metaphysis are large and tortuous, and consequently at this region the blood flows slowly and any blood borne organisms are apt to be arrested.

The above description applies to typical long bones. In short and irregular bones the blood supply is somewhat different, and is derived principally from periosteal arteries, and to a less extent from one or more "nutrient" arteries. In the short long bones of the hand and foot the blood supply is derived principally from single nutrient arteries, which pierce the shaft and immediately break up into fine twigs. In infancy these bones possess no metaphyses, and consequently diseases such as tuberculosis originate in the centre of the shaft.

**Microscopic Structure of Bone** All parts of a bone are pervaded by channels of various sizes, relatively few in compact bone, numerous in cancellous bone. The large channels are the *Haversian canals*. These run mainly in the long axis of the bone, and they contain connective tissue, blood vessels, nerve filaments, and lymph channels. In addition, the large channels of cancellous bone contain marrow elements. Around the Haversian canals and communicating with them are the *lacunæ* which contain the bone cells, the branched cells of the connective tissue framework which preside over the nutrition and metabolism of the bone. The branching processes of these cells occupy minute channels or *canaliculi*, which ramify in all parts of the bone.

Around each Haversian canal the bone is arranged in concentric lamellæ, which with the canal, the lacunæ and their canaliculi constitute a *Haversian system*. Near the surface of the bone a different arrangement obtains. The lamellæ here lie parallel to the surface and are nourished by blood vessels of periosteal origin lying in the Volkmann's canals. These superficial lamellæ are pierced by perforating fibres of white fibrous and elastic tissue, which are connected with the periosteum and with the insertions of tendons and ligaments.

It will be noted how admirably a bone is constructed for its essential function of providing a rigid support. The Haversian systems arranged longitudinally, and the superficial lamellæ arranged parallel to the surface, give longitudinal stability, whilst the fibrous and elastic tissues give elasticity and strength. Bone may be compared to a plaster of Paris bandage, in which the gauze is represented by the fibrous and cellular parts of the bone and the plaster by the calcareous part. Incinerate a bone and only the calcareous material is left, place it in strong mineral acids and only the fibrous structure remains.

## DISEASES OF BONES

It should be observed that in spite of its hardness and density bone is a very vascular tissue, unlike that other component of the skeleton, cartilage. It is for this reason that bone so readily undergoes decalcification or other changes in response to metabolic or hormonal influences, or from the effects of local lesions such as tumours, aneurysms, or infections.

### THE GROWTH OF BONE

The majority of bones are formed in cartilage, and only a few, including the bones of the calvarium and some of the facial bones, are developed in membrane. Since bone formed in cartilage is especially subject to diseases, the process of endochondral ossification will be described in some detail.

Bone formation starts in the clavicle in the fifth week of intra uterine life, and in many other bones a short time later. The ossifying process begins near the midpoint of the bone and spreads thence through the whole diaphysis. Secondary centres of ossification appear later in the epiphyses and apophyses, and later fuse with the shaft.

Microscopically, in the process of ossification several distinct changes may be recognized whereby the cartilage first proliferates, then becomes calcified and finally is replaced by vascular bone forming connective tissue. The cartilage itself is not ossified, it merely provides a cellular matrix suitable for the growth of osteogenic connective tissue. The stages of bone formation may be recognized as three distinct zones in a growing bone, extending from the pre formed hyaline cartilage at one end to the completed bone at the other. The first zone is the *zone of proliferation of cartilage*. The cartilage cells increase in number and in size, and they become arranged in columns disposed in the long axis of the bone. The number of columns is constant in each bone. The second zone is the *zone of provisional calcification*, where calcium phosphate is deposited from the blood stream forming a narrow band extending the whole width of the bone so that when the bone is cut longitudinally it appears as a thin white transverse line. In diseases associated with deficient calcification this white line may be absent or replaced by a broad irregular area of greyish colour. The third zone is the *zone of replacement of cartilage by osteogenic tissue*. Capillary vessels grow out in regular columns from vessels in the existing bone into the band of calcified cartilage, and the new bone is formed around and between these vessels. Along with the vessels come small dark staining cells or osteoblasts. These are specialized connective tissue cells which are generally regarded as the specific bone forming cells, their function being to elaborate an osteoid matrix in which calcium is deposited to produce bone as we recognize it. When the bone has been formed the osteoblasts remain as "bone cells".

### THE REMODELLING PROCESS

Bone is not an inert and immutable framework, but a living tissue adjusted to meet the varied forces imposed upon it. This is evidenced

most strikingly during growth of the skeleton. The primordial bone at the metaphysis is relatively soft and vascular, and is not fitted to meet the stresses imposed by gravity and muscular action. It is adapted to these requirements by a process known as remodelling, by which the bone becomes compact or cancellous according to the functional requirements of the part. The remodelling process is the factor that decides the ratio between size, stability and strength in bones and is probably brought about by many agencies, including chemical organizers, the restraining effect of the periosteum, and the action of the muscles. The young bone at the metaphysis is often more bulky than future requirements demand, and by the process of remodelling it is reduced in quantity and increased in density to attain the requisite thickness and compactness of the shaft. Examples of failure of the remodelling process during skeletal growth are found in the dystrophies now grouped under the title *diaphyseal aclasis* (see p. 129).

In adult life the remodelling process effects alterations in the structure of any part of a bone, according to its special needs. An outstanding example of this is seen when the statics of a bone is altered by the union of a fracture in faulty alignment. To meet the altered axis of weight bearing the bone and callus assume a dense lamellated structure in the new lines of pressure, whereas parts subjected to less stress are relatively porous.

## RELATION OF BONE TO THE METABOLISM OF CALCIUM AND PHOSPHORUS

The elements calcium and phosphorus have an important part in many metabolic processes, and are essential for such basic activities as the mechanism of the heart beat, the contractility of muscles, the irritability of nerves, and the regulation of acid base reactions. The role of the skeleton is to act as a storehouse for these elements, and thus to ensure a constant level in the blood so that it is not surprising that any disease which affects calcium and phosphorus metabolism is reflected in the bones.

Calcium and phosphorus are obtained from the food by absorption in the alimentary tract, and such portions as are not utilized are eliminated in the faeces and urine.

Calcium is absorbable only in soluble form. Its absorption is therefore impaired when there is an excess of phosphates or alkalis in the diet, which leads to precipitation of the calcium, or when fat digestion is incomplete, a condition leading to precipitation of calcium soaps. Vitamin D, in virtue of its rôle in facilitating fat digestion, is also a necessary factor in the absorption of calcium.

Calcium is held in solution in the blood in a concentration far in excess of its ordinary chemical solubility. Part of it is adsorbed on to the serum proteins. The remainder is in ionic form, and is probably maintained in supersaturated solution by the agency of the parathyroid hormone.

The calcium and phosphate ions in the blood are in chemical equilibrium with the solid calcium phosphate of the bones, and are therefore



subject to the laws of ionic dissociation. Consequently, an increase in ionic phosphate in the serum leads to diminution of the serum calcium and to deposition of calcium phosphate in the bones. Conversely, a reduction of the ionic phosphate leads to increase in serum calcium and to mobilization of calcium phosphate from the bones. This latter effect is seen clinically in cases of acidosis, where the buffer phosphate is excreted and consequently decalcification of the skeleton is brought about. It is seen also in hyperparathyroidism, for the effect of an increase of parathormone is to remove phosphate from the blood and thus to cause decalcification.

Calcium metabolism is thus dependent upon a great number of factors, adequate diet, unimpaired fat digestion, sufficiency of vitamin D, maintenance of the hydrogen ion concentration of the blood, and proper functioning of the parathyroid glands. The internal secretions of the pituitary and thyroid glands also play some part in the process. Thus pituitary disease leads to gigantism and acromegaly, and sometimes marked skeletal decalcification. Thyroid dysfunction causes bone atrophy in exophthalmic goitre and dwarfing in cretinism. Even the sex glands are related in some way to the whole process. Their connexion is not obvious in the human, but in animals it is sometimes of great biological importance. In the stag, for example, the growth and subsequent casting of the antlers is intimately related to the seasonal sex cycles, and, as John Hunter observed, if the animal be castrated its antlers are shed prematurely.

It seems probable that the mineral salts of bone are held in a complex molecule which includes calcium phosphate and carbonate along with magnesium, sodium, potassium, chloride, fluoride and hydroxyl groups.

Robison has shown that the deposition of calcium phosphate from the soluble salts in the tissue fluids is effected through the agency of an enzyme, *phosphatase*. This enzyme has been shown to be present in greatest concentration in tissues in which ossification is actively proceeding. It acts primarily by hydrolysing the soluble phosphoric ester, with liberation of free organic phosphate. If a sufficiency of calcium salts be present, the resulting increase in the concentration of phosphate ions leads in turn to precipitation of the complex calcium carbonate phosphate molecule. The activity of phosphatase appears to depend upon the hydrogen ion concentration of the blood, and is greatest when the pH is deflected towards the acid side—the condition normally present in growing bones or in healing fractures.

### THE RÔLE OF THE PERIOSTEUM

In 1741, Duhamel, a French squire of scientific inclination, making use of the recently discovered method of staining bones *in vivo* by the oral administration of the dye madder, found that increase in girth of a bone is due to the formation of layer upon layer of bone under the periosteum, just as the increase in diameter of a tree trunk is due to the activity of its cambium layer. On the basis of this experi-

mental observation he formulated the theory of the essential osteogenic function of the periosteum, a theory which ever since has been the subject of controversy.

Ollier, of Lyons, was the great protagonist of Duhamel's theory. In his classical work which appeared in 1867, and which contained many valuable observations on the growth of bone, he claimed that the periosteum of young subjects is capable of osteogenesis even when separated from the bone and buried in muscle, and he showed that in adults also the periosteum continues to exercise this function when stimulated by trauma or by infection.

On the other hand, there is the view, which Macewen has powerfully supported, that the periosteum has no bone forming property, but is merely a vascular fibrous membrane whose function is to limit bone growth. Macewen, as a result of a series of masterly experiments and observations, came to the following conclusions: (1) That the periosteal flaps described by Ollier were not osteogenic unless spicules of bone adhered to them, (2) that the life, growth, and repair of a bone are not affected by removal of its entire periosteum, and (3) that after subperiosteal resection of the shaft of a bone the new bone is formed, not by the periosteum, but by a dual process of proliferation from the cut bone ends and (in youth) of compensatory overgrowth of the metaphyses. This last conclusion was suggested by experiments in which the bone ends after partial diaphysectomy were covered by metal caps, after six weeks the defect was filled by new bone, and at this time the caps were found to be approximated, indicating that the new bone was derived not from the periosteum but from what remained of the original diaphysis.

As has been stated already, the "battle of the periosteum" is not yet concluded, although many of the apparent discrepancies have been settled. It has been suggested that the periosteum may best be regarded as a double layered membrane. The outer layer is thick and fibrous, and its function is one of limiting and vascularizing. The inner or "cambium" layer, which is active only in youth, is a thin layer of delicate connective tissue containing numerous osteoblasts, and its function is osteogenic. This cambium layer is more intimately connected with the cortical bone, from which it takes origin than with the fibrous periosteum, and it may with advantage be termed the *epiosteum* (Hey Groves).



FIG 44. Regeneration of bone after partial diaphysectomy. A radiogram taken four months after subperiosteal resection of a part of the tibial diaphysis. Note the thick mass of new bone already sclerosed which has grown from the upper fragment. A thin wedge of bone from the lower fragment extends proximally under the periosteum.

Whatever views are held regarding the function of the periosteum, it is beyond doubt that it takes a very important part in pathological processes affecting bone. The periosteum acts as a capsule or restraining membrane to bone, and a bone cannot alter its shape or exceed its normal limits unless the periosteum be removed, raised, or stripped. What sometimes is called "expansion of bone" suggests that bone is distended by pressure from within but as bone is a rigid structure such a belief is obviously unacceptable. Expansion of bone is dependent on the periosteum being raised by some agency, such as trauma or temporary or recurrent effusions, and a simultaneous softening and decalcification of the underlying bone.

### MECHANISM OF BONE FORMATION AND RESORPTION

Since Goodsir in 1845 first applied the microscope to the study of bone growth, it has been assumed almost universally that bone is a product of the vital activity of specific cells known as *osteoblasts*. These are polygonal cells, with dark staining protoplasm, which show a tendency to arrange themselves in layers in apposition to the bone trabeculae. In youth the osteoblasts are present in large numbers under the periosteum and at the metaphysis, the two regions where bone formation proceeds most actively. They are present also, in either youth or adult life, at nearly all sites of osteogenesis, physiological or pathological.

Most pathologists prefer to regard the osteoblast as a specific type of mesoblastic cell whose purpose is to provide a matrix (ossein or osteoid tissue) for bone, just as the fibroblast is specialised to produce collagen fibrils. Probably the osteoblasts take no part in the deposition of calcium, which is determined more likely by physico-chemical processes.

*Resorption of bone* consists essentially in the conversion of the insoluble crystalline calcium phosphate of bone into soluble or colloidal calcium phosphate. It is generally accepted that resorption is effected in part by *halisteresis*—a physico-chemical process in which the calcium is withdrawn by the agency of the body fluids—and in part by the vital activity of the osteoclast cells. These osteoclast cells are multinucleated giant cells with the characteristics of foreign body giant cells, and they are present around many sites of physiological or pathological bone resorption. They are variously regarded as phagocytic wandering cells, or as modified osteoblasts.

Leriche and Policard have suggested that bone results from a metaplasia or metamorphosis of primitive mesenchyme, which is brought about by a combination of environmental or physico-chemical factors, rather than by the action of any specifically endowed cells. They point out that bone formation occurs always in young mesenchymal tissue sustained in certain physical characteristics, and this tissue they call an *ossifiable medium*. Bone formation depends first upon the presence of such an ossifiable medium, and, secondly, upon the presence of an adequate supply of readily assimilable calcium. According to this hypothesis ossification depends upon local adjustments of the circulation, and is independent of the action of osteoblasts.

In our opinion the greatest importance of the work of Leriche and Policard lies in the prominence they give to the action of circulatory changes in modifying the behaviour of bone. In general it may be stated that excessive blood supply (hyperemia) is associated with bone resorption, and conversely diminution in blood supply, other things being equal, with sclerosis. These views regarding the changes induced by alteration of the vascularity of bone serve as a valuable means of interpretation for many pathological phenomena, especially in radiological studies of bone diseases.

### HETEROTOPIC OSSIFICATION

The development of bone in tissues remote from the skeleton is a rare but interesting process, the reason for which has provided considerable speculation. Heterotopic ossification has been observed quite frequently in the scar of an old abdominal incision, and it may occur in an old hæmatoma, in the wall of an aneurysm, in tumours, and in many other situations.

Ossification in the perichondrium of calcified costal cartilages is another example of the same phenomenon. It is most common in the upper and more stationary ribs. It usually affects elderly people, but it may occur in young subjects, especially if they suffer from chronic pulmonary disease that leads to fixation of the chest wall. The ossification begins close to the sternum and is first apparent near the surface of the cartilage.

In "myositis ossificans progressiva," bone formation of a heterotopic character is found on a large scale. The new bone is preceded by calcification and by a proliferative change in the fibrous connective tissues of the muscle (see p. 214).

The bone formation occurs always in relation to fibrous connective tissues and in structures that may be regarded as in a state of functional disuse or death, and it is always preceded by deposition of lime salts such as is of common occurrence in healed tuberculous nodules in lymph glands, blood vessels, or in scar tissue in many other situations.

In the past heterotopic ossification was generally attributed to the activity of osteoblasts derived from local or distant sources. Thus ossification in the abdominal wall was ascribed to injury to the pubis or xiphisternum, with consequent liberation of osteoblasts, whereas ossification in other situations was thought to be due to the action of osteoblasts migrating from the blood stream into the injured tissues.

The present day view is that the presence of specific cells (osteoblasts) is not essential, and that if the requisite conditions of vascularity and calcium supply are present any primitive mesenchymal cells may assume the osteoblastic function.

### UNION IN FRACTURES

It is customary to describe three stages in the repair of a fractured bone: (1) the stage of blood clot and granulation tissue, (2) the stage of callus, and (3) the stage of ossification. These divisions, though rather arbitrary, serve to mark the various phases of healing in bone.

Soon after fracture the bone ends and lacerated tissues about them are surrounded and infiltrated by blood-clot, which may vary in amount and in distribution in different fractures. Newly formed capillaries invade the clot, along with phagocytic cells and fibroblasts, which slowly replace the clot by a vascular granulation tissue. If the fracture is examined after about ten days the tissues will be found to be very gelatinous, and a clear, slightly pink jelly covering the ends of the bones will be observed. A little later calcific material is deposited in the exudate, which, at this stage, is sometimes known as the pro-callus.

In the intermediate stage of repair islands of new bone appear in the calcium-infiltrated granulation tissue, and to this mass of newly formed bone and proliferated tissues the name callus is given. The early callus is usually soft and forms a roughly globular or spherical mass between and at the ends of the bones as well as for a variable distance in the surrounding soft parts. The amount of callus and its disposition in relation to the bone ends is very variable and is influenced by many local factors. The portion outside the bone and beneath the true periosteum is known as the external callus; that which plugs the interior of the bones is the internal callus; and that connecting the actual fragments is the intermediate callus. When healing is complete only the intermediate callus persists, and throughout life it shows a slightly greater density than the adjacent bone.

The amount of callus which is deposited at the site of fracture is very variable. It depends, among other things, on the site of the fracture and the degree of damage to the bone. Thus it is greater in oblique or comminuted fractures than after simple transverse fractures or after osteotomy. In greenstick fractures the amount of callus tends to be relatively large, probably as a result of hæmorrhage from the vascular periosteum. In fractures of the skull there is little or no callus formation. The amount of callus tends to be increased by movement during the repair of the fracture.

Evidence of bone resorption may be very readily seen in radiograms taken at intervals after fracture. They show decalcification and rarefaction of the bones at the site of fracture and for a variable distance beyond it. The result of such resorption is appreciated if the fracture is exposed at operation, when it is found that after about ten days the bone ends have lost their sharp spiculation, and are more porous and, as a result, less readily adaptable to one another. If looked for, the jelly-like pre-osseous substance may be found on the fragments; it may be regarded as the primitive callus in which deposition of lime salts is to occur prior to actual bone formation. New bone is rarely apparent until about the tenth day, and twenty-five days usually elapse before the callus becomes firm. Toughening of the callus is probably caused by the gradual return of the local circulatory conditions to normal. At an early stage of the formation of a mass of callus a thick and oedematous covering of periosteum is found. Later it becomes tough and fibrous and forms an investing membrane at the site of union.

Delayed union or non-union is often met with in the long bones, and there are some sites at which it is especially common. These are the neck of the femur in old subjects, the distal third of the ulna, the distal

part of the tibia, the middle of the shaft of the humerus, the patella and the olecranon. Non union is very common in fracture of the carpal navicular and of the calcarii.

When the fragments of bone are exposed in a case of non union of long standing their ends are generally found soft, spongy and rarefied. Sometimes absorption has taken place to such an extent that a considerable gap separates the fragments. In some instances, especially those associated with pseudarthrosis, there is sclerosis of the ends of the bones, especially of the distal fragment which may be cup shaped. Sometimes an encysted collection of serous fluid is found within the fibrous capsule uniting the bones.

Non union may be attributable to constitutional or local causes. Constitutional predisposing causes are not well defined. It is generally stated that severe anemia, wasting diseases, syphilis, diabetes mellitus and chronic renal disease predispose to non union, but it seems probable that their importance has been over estimated.

Local predisposing causes of non union are of three main varieties (1) mechanical hindrance to the approximation of the fragments and their union by callus, (2) interference with the normal biological process of new bone formation, and (3) inadequate immobilization. Sometimes the factors are combined.

(1) Mechanical hindrance to the approximation of the fragments may result from wide separation of the fragments or from interposition of soft tissues such as muscle and fascia. Actual new bone formation may be attempted, and the bone may invade the interposed muscle, but it is deposited in the axis of the muscle fibres and lies at right angles to the fragments, and is thus of no value in cementing the fracture.

(2) Interference with the normal biological process may result from infection, pre existing disease in the bone, derangements of the local circulation (as by rupture of a nutrient artery), and other factors.

Infection is an important cause of non union and accounts for the frequency of this complication in compound fractures. The presence of a foreign body may further militate against repair. Infection may disturb the processes of union in several ways (a) by causing necrosis of the fragments, (b) by causing destruction of the young bone forming elements, (c) by delaying the normal process of new bone production to such a period that some of the essential factors for osteogenesis are lost. Such is the part played by fairly severe infection, but in the presence of a mild degree of infection, union is often very firm and attended by an excess of callus.

Pre existing disease of bone such as cysts, tumours, or osteomyelitis may determine non union, but it is remarkable that not infrequently union may occur even in the presence of extensive local disease.

(3) In the repair of some fractures a slight degree of movement is regarded as beneficial, and many surgeons encourage active movement of a fractured bone from the onset. None the less, there are many sites at which this practice must be regarded as injurious and likely to promote non union. Many indeed believe that the most fruitful source of non union is faulty immobilization, especially such as permits of repeated slight shearing or torsional strain at the bone ends,

and it is significant that those fractures which fail to unite are precisely those which are difficult to immobilize completely. Experience in the management of common fractures such as that of the carpal navicular and the femoral neck in old subjects has afforded convincing evidence of the importance of securing firm fixation of the fragments and protection of the developing callus. In intracapsular non impacted fracture of the neck of the femur non union is almost invariable unless immobilization is obtained. Following immobilization, secured preferably by operative means, firm union results in a considerable number of cases. Non union at the neck of the femur is associated usually with marked absorption of bone locally and cupping of the distal fragment, which, formerly, was attributed to atrophy as a result of rupture of the nutrient vessels, but, more likely, the disappearance of bone and the non union are due to disturbance of the callus induced by the trauma of recurring slight movement, or to aseptic necrosis of the proximal fragment.

In fracture of the carpal navicular, union is uncertain unless movement of the wrist and carpal joints is abolished during treatment. The non union resulting from too early resumption of movement can generally be overcome by prolonged immobilization.

In some situations it appears that excessive mechanical traction may be responsible for delayed union as a result of undue separation of the bone ends.

### TRANSPLANTATION OF BONE

Bone transplants are commonly employed in orthopædic and plastic surgery. They are required most frequently to restore continuity and to promote union of a fractured bone. Sometimes they are used to bridge the gap resulting from injury, necrosis or operative interference. In other instances they are of service to immobilize a tuberculous vertebra, to deepen the acetabulum in congenital dislocation of the hip, or to stabilize a flail joint.

The transplant may consist of living or of dead bone. Living bone may be derived from the same subject (autoplastic) or from another individual of the same species (homoplastic). Dead bone is usually derived from another species, and is conveniently obtained from beef bone that has been boiled and suitably shaped. Occasionally, portions of ivory in the form of pegs or nails are employed.

Autoplastic transplants are most generally useful. They may be derived from near the site of intended implantation, for example, the bone adjoining a fracture, or from some other part of the skeleton such as the subcutaneous surface of the tibia, the proximal end of the fibula, or one of the ribs. A single large transplant or a number of small fragments, "bone chips", may be used. Custom, circumstance and ingenuity play a prominent part in determining the site for obtaining the transplant, and the ease with which a transplant may be taken from the tibia makes this the favourite source. The ribs, though accessible and of suitable curvature for many purposes (e.g., repair of

defects in the skull), do not provide satisfactory transplants on account of their lack of substantial cortex

**The Fate of Bone Transplants** This is a problem on which there is no general agreement. Transplants of dead bone (such as beef bone or ivory) are generally believed to subserve two principal functions (1) to give stability at the site of implantation, and (2) to act as osteo-conductive agents, scaffoldings along which new bone may be deposited. The dead transplant acts as a foreign body and stimulates a reaction on the part of the surrounding tissues.

Transplants of living bone give stability and act as osteo-conductive agents, and in addition, it is believed, they encourage osteogenesis. It is believed that they serve this purpose best when transplanted with the periosteum retained.

The viability of a living transplant is a subject of controversy. The view most widely held is that a thin superficial layer of the transplant survives, the cells of this part acquiring nourishment from tissue fluids and effused blood serum. The remainder of the transplant dies and then functions as a dead transplant. If the transplant be examined forty to sixty days after its implantation it will be found to be rarefied, and the Haversian canals are wider than normal, and are invaded by granulation tissue and newly formed blood vessels.

Radiological studies show that in most cases the transplanted bone is gradually absorbed, and simultaneously new bone is formed in the tissues around it. It must be noted, however, that in some bone transplants, notably pegs inserted into the marrow cavity and transplants used for spinal fixation, the shadow of the transplant is visible for many years. In such cases it must be conceded that the transplant either has lived unchanged or after serving its purpose has become incorporated in the tissues as a foreign body.

## OSTEOMYELITIS

Any inflammatory process involving bone and marrow may be called osteomyelitis, but the unqualified term is generally restricted to non-tuberculous lesions due to pyogenic micro-organisms. The disease may follow direct infection from local sources, as in compound fractures or from an open wound, or it may result from hæmatogenous infection derived from distant sources. The hæmatogenous type will be described first. It is principally a disease of childhood or of adolescence, and when it does affect adults the pathological process is somewhat modified.

## ACUTE OSTEOMYELITIS

This is a common disease, and, if untreated, a serious one. Boys are affected three times more frequently than girls, and most often between the ages of three and ten years.

In the great majority of cases the infecting organism is the staphylococcus aureus. The staphylococcus albus or streptococci are sometimes the causal agents, and occasionally in young children pneumo-



cocci. The origin of the infection is not always obvious. Sometimes a boil or septic abrasion in the skin is present, sometimes the tonsils are inflamed, but very frequently it is impossible to detect a primary focus.

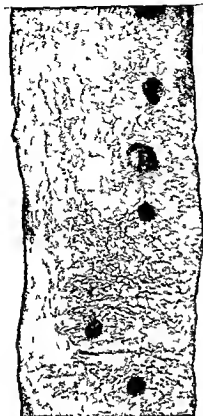


FIG. 45. Septic osteomyelitis of the tibia of three and a half years duration in a man aged twenty years. There is a massive involucrum perforated by numerous cloacae through which a large sequestrum may be seen.

(Museum of Royal College of Surgeons of Edinburgh.)

In most cases the disease appears to start as a septicæmia. The circulating organisms then settle in favourable situations in the bones and there lead to an acute suppurative inflammation. Often there is a history of a recent minor injury to the affected bone, and probably a small traumatic hæmorrhage forms the nidus favourable to the growth of the infecting organism.

The septicæmic phase may be of short duration, or it may be prolonged during several days. In the latter event multiple foci may develop in several bones, simultaneously or in succession.

**The Local Lesion.** The bone focus is generally situated in the metaphysis, which is the region of most active growth and consists of immature vascular bone, easily traumatized.

The infection then spreads (1) to the surface, causing subperiosteal effusion, (2) down the medullary canal, and (3) rarely through the epiphysis. The infection traverses the Haversian and Volkmann's canals in the cortex, and erupts under the periosteum, raising it off the bone surface. Since the periosteum is closely attached to

the circumference at the epiphyseal cartilage the infection does not spread towards the joint except in certain regions, such as the hip, where the metaphysis is intra-articular. When the periosteum is elevated from a wide area the small periosteal arteries become obliterated, and the blood supply to the cortex is impaired. Superficial portions of the bone undergo necrosis and may later form sequestra. Rarely the principal nutrient artery to the bone may be occluded by thrombosis, and then the greater part of the diaphysis dies.

Fortunately, however, this extensive necrosis is much less frequent than examination of museum specimens suggests.

In cases treated promptly and adequately by penicillin necrosis

is rare but radiological examination shows widespread rarefaction of the bone, which may persist for a long time. In such cases, probably owing to hyperæmia, the lengthwise growth of the bone at its metaphysis may be greatly accelerated.

In untreated cases if necrosis occurs, the dead portion of bone is at first continuous with the living but demarcation is not long delayed, its surface, denuded of periosteum, is smooth and shiny and white, when percussed it emits a "dead" sound, and when pierced it does not bleed. Around the margins of the dead bone there rapidly develops a foreign body reaction, and small portions of necrotic bone may be completely absorbed, but large ones remain until extruded or removed by operation.

The sequestrum, when completely loosened from its attachments, lies in a cavity in the bone, and interferes with healing, often for years. Secondary infection is an important factor in aggravating and prolonging suppuration.

### Acute Osteomyelitis in Adults

Osteomyelitis is much less common in adults than in children, and, since the general resistance to staphylococcal infection seems to be raised the disease is neither so rapid in progress nor so uniform in character. In adults there is no metaphysis, and such local predisposing factors as result from the rapid growth of bone are absent. Consequently, any part of a bone may be affected. Trauma often seems to be a definite predisposing factor, and such exposed regions as the medial surface of the tibia are likely to be affected. The course of the disease is slow and the symptoms are less severe.

### Acute Osteomyelitis in Special Situations

It is noteworthy that the more peripheral the bone affected the less severe is the disease. The site most commonly affected, the proximal end of the tibial diaphysis, is fortunately one of the least dangerous, and the superficial position of the bone facilitates early recognition of the disease. When the upper end of the femur is attacked constitutional features are usually pronounced, and in early childhood the hip joint is often involved. At the distal part of the femur the loose attachment of the periosteum on the underlying cancellous bone favours early abscess formation in the popliteal fossa, and from deprivation of blood supply to the bone massive sequestration was formerly a common feature.

*Osteomyelitis of the vertebrae* is a rare disease, affecting adults more



FIG. 46. Osteomyelitis of the tibia. Almost the whole diaphysis has undergone necrosis and is seen as a smooth shiny sequestrum, surrounded by a rough, irregular involucrum.

(Museum of Royal College of Surgeons of Edinburgh.)

often than children. If the infection arises in a spinous process or lamina the pus may make its way to the surface and do little damage, but if the vertebral body is diseased the condition is more serious. The deep situation, the lack of localizing symptoms, and the great constitutional disturbance combine to obscure the diagnosis, complications from spread of infection to vital structures rapidly supervene.

In the cervical region an abscess which develops in the prevertebral space may pass to the mediastinum, in the thoracic region mediastinal cellulitis and empyema commonly occur, and in the lumbar region a rapidly extending psoas or an acute perinephric abscess may form. Finally, the infection may pass towards the spinal canal and give rise to spinal meningitis.

*Osteomyelitis of the pelvic bones* is a serious disease and the profound constitutional disturbance usually overshadows the local features of the infection. Any of the bones may be affected, usually in relation to one of the many epiphyseal cartilages, especially the pubo-ischial. From the ilium an abscess may develop on the pelvic aspect or superficially under cover of the gluteal muscles. From the pubis the abscess may rupture into the bladder, and a sequestrum may even perforate it.

### CHRONIC OSTEOMYELITIS

Chronic osteomyelitis is usually a legacy of the acute disease, but it may arise insidiously and pursue a slow course.

In the type that succeeds the acute disease there are usually one or more sinuses communicating with the exterior. The surface of the bone is very irregular, either over its whole extent or over one end of the shaft, and it is thickened by new subperiosteal bone. At the metaphysis, or extending for a variable distance within the bone, there is an abscess cavity, sometimes of considerable dimensions. Around the cavity the bone becomes greatly increased in density, and the neighbouring marrow cavity is obliterated by new bone formation. Sometimes there are several small cavities within the sclerotic bone.

Apart from lingering or relapsing infection the principal factors that prevent healing and maintain the disease in its chronic state are the rigidity of the wall of the bone cavity, and/or the presence of one or more sequestra within it. Small sequestra may be discharged at intervals through sinuses, and sometimes small fragments of bone migrate to the surface many years after the original infection, even after healing of the skin. Massive sequestra are usually entrapped within the involucrum and until liberated constitute a source of continued suppuration.

*The insidious form* of chronic osteomyelitis due to staphylococcal infection is somewhat rare. It usually affects adults. Scanty or avirulent organisms carried by the blood stream are deposited, usually at the metaphysis, and here give rise to a low grade inflammatory reaction. The so-called *Brodie's abscess* commonly results. This is an abscess in the bone, most commonly in the proximal end of the tibia, less often in the distal end or in the femur or the humerus, or more rarely elsewhere. The cavity lies in the central axis of the bone

and is at first close to the metaphysis, but may be removed from it as the bone grows. The abscess is usually of small size, a centimetre or less in diameter, buried in sclerosed bone. Overlying it, the surface of the bone is often irregular from new subperiosteal proliferation. The abscess sometimes remains for years with little sign of activity, and in these circumstances it often contains sterile gelatinous granulations and is surrounded by a fibrous wall. No sequestrum is present as a rule. With more active infection the abscess may enlarge and become filled with thick pus, from which organisms may be cultivated.

A Brodie's abscess may remain unrecognized for a long time, occasionally for many years. Pain of a dull aching or boring nature is felt in the bone, especially at night, and the neighbouring joint may be the seat of recurring effusion. A striking feature is the great sensitiveness of the bone overlying the abscess. A radiogram displays the cavity surrounded by dense bone.

**Chronic Hypertrophic Osteomyelitis.** Osteomyelitis may be chronic from the onset and may then result in extensive hypertrophic changes in the affected part, usually one of the long bones. The infecting organism is usually the staphylococcus aureus. The disease tends to affect young adults, but sometimes it occurs in later life. The commonest sites for this somewhat rare type of osteomyelitis are the lower end of the femur, the upper end of the humerus, and the tibia. It has been observed also in the clavicle and in the radius.

When seen at operation the affected part of the diaphysis shows a fusiform thickening due to the deposition of new lamellae of bone beneath the periosteum. The periosteum and bone at the affected area are abnormally vascular, and the marrow cavity may be obliterated. Generally there is no suppuration nor sequestrum formation, but occasionally a small abscess is encountered. The infecting organism can usually be cultivated from excised bone chips.

The condition is associated with aching pain and slight swelling of the affected limb, and movements of the neighbouring joint are often restricted and painful. Intermittent slight rises of temperature are often noted, and examination of the blood shows a slight polymorphonuclear leucocytosis, seldom higher than 14,000 cells per c mm.

The importance of this form of osteomyelitis is its resemblance to sarcoma, and very careful and repeated radiological examinations or even biopsy may be required to establish its nature.

### Typhoid Osteomyelitis

In the septicæmic stage of typhoid fever the bacilli appear to find the bone marrow a favourable nidus, and it has been shown that they may be cultivated from this tissue almost as frequently as from the spleen. Moreover, they may remain latent in the marrow long after the original disease has subsided, yet cause no symptom until awakened to activity, perhaps by some mild trauma or other disposing factor.

Typhoid osteomyelitis arises usually from four to six weeks after the onset of the fever, but it may appear months or even years later. The ribs are affected most often, especially in the neighbourhood of the costo chondral junctions, and the cartilage close by may also be



FIG 47 A macerated specimen of the distal two-thirds of the left tibia and fibula illustrating the development of osteophytes which commonly occurs in a chronic leg ulcer. The new bone formation is most abundant at sites of muscular attachment and in the plane of the interosseous membrane.

(Museum of Royal College of Surgeons of Edinburgh.)

affected. In other cases the sternum, the bones of the pelvis and the spine, the ulna or the tibia may be involved. The disease takes a mild course, either insidious in progress or with recurring mild exacerbations, and there is usually little new bone formation, and only slight tendency to the formation of sequestra. Sometimes the bacilla are present in pure culture, and the pus is then scanty and rust coloured from altered blood. More often there is mixed infection with *B. coli* or *staphylococci*, and the pus is then of the type characteristic of these organisms.

### Osteomyelitis Following Local Infection

Any open wound communicating with a bone, a compound fracture, burn, or an abscess in the neighbourhood of a bone, is apt to lead to some degree of osteomyelitis. The extent and severity of the infection vary in different cases, depending partly upon the nature and virulence of the infecting organisms, and partly upon such other factors as the amount of damage to the soft parts and the amount of foreign material introduced. The severest lesions are those associated with much devitalization of the bone or soft tissues, as in gunshot wounds and street accidents, and if a virulent infection is introduced the whole bone may undergo necrosis. Minor injuries with slight infection may lead merely to superficial inflammation (periostitis) or perhaps to necrosis of small flakes of cortical bone.

A classical example is *osteomyelitis of an amputation stump*, and in what may be called the amputation era of surgery many specimens of this affection found their way into museums. The open medullary canal formed a ready route of entry for organisms, and these were spread widely along the bone or remained near its extremity. In the latter case a sequestrum usually resulted, which involved a short annular portion

of the cortex, often with a longer tapering portion of cancellous bone

### Boae Changes resulting from Adjacent Inflammatioa

The bones adjacent to an acute inflammatory process may share in the regional hyperæmia and undergo considerable osteoporosis which, in some situations may lead to grave effects. One of the most notable examples of this process has been observed in the upper cervical vertebræ in association with acute inflammatory lesions of the pharynx and of the glands of the neck. The hyperæmic decalcification of the vertebræ particularly of the atlas and axis may allow of loosening or separation of the intervertebral ligaments resulting in forward luxation or dislocation of the atlas. The displacement may occur spontaneously or from trivial violence. It may occur without complications but in some cases it has led to compression of the cord giving rise to quadriplegia, in others the compression has been fatal.

When the local inflammatory process is less acute as for example in a chronic ulcer of the leg the reaction in the underlying bones is quite different. The inflammatory hyperæmia which may vary in intensity from time to time leads to a proliferative reaction in the periosteum and effusion beneath it. New bone formation occurs irregularly as osteophytic outgrowths beneath the periosteum and in the interosseous membrane (Fig 47) and its form and distribution may be modified by gravity or by muscular action.

## SYPHILIS OF BONES

The bones may be affected in both the secondary and tertiary stages of acquired syphilis or in inherited syphilis. Nowadays the disease is seldom seen.

In general, the pathology is fundamentally the same as that of syphilis in other tissues but modified by the special anatomical and physiological attributes of the bone. The bone at the site of the lesion may undergo temporary decalcification and partial destruction but later when the vascularity of the part diminishes it is apt to become sclerosed.

The bones most liable to syphilitic lesions are the tibia, sternum, ulna, clavicle and the skull. In the long bones the lesions are situated usually in the diaphyses and consequently syphilis of the bones, unlike tuberculosis, rarely leads to joint involvement.

**Secondary Stage.** In the secondary stage of acquired syphilis the bones are liable to be involved after the period of the skin eruptions. The tibia is affected most often. Commonly there is a periostitis which is mild and transient. The periosteum is infiltrated with round cells and becomes painful and tender to pressure. In some cases multiple areas of fibrous tissue develop—*periosteal nodes*—which, in superficially placed bones like the tibia, may be obvious as localised tender swellings.

**Tertiary Stage.** In the tertiary stage of acquired syphilis the bones may be affected either by localized gummata (single or multiple) or by a diffuse gummatous osteo periostitis.

*Gummata* affect the tibia often, and are situated generally at the proximal third of the diaphysis. The sternum also is affected frequently. Sometimes the gumma softens in the centre and breaks down to form an abscess or ulcer of characteristic appearance, with an indurated, sharply defined, "punched-out" margin and a yellowish sloughing base. The ulcer provides an avenue for superadded infection, and a septic osteomyelitis may then develop, which may result in necrosis of the bone and sequestrum-formation. Eventually an ulcerated gumma may heal, leaving a glazed, yellow-coloured scar. Gummatous ulcers develop most often in relation to the bones of the skull, and super-added infection may then lead to suppuration inside the cranium.

*Diffuse gummatous osteo-periostitis* results from an infiltration similar to the localized infiltration of a gumma. The diaphysis of the tibia is affected frequently. The bone eventually undergoes sclerosis, and much new bone of dense structure is formed, both on the surface of the shaft and within its marrow cavity. The bone is

greatly increased in weight. The periosteum is thickened, and adheres firmly to the surface of the bone, which is grooved and irregular. The marrow cavity is encroached upon and may be totally obliterated.

#### Inherited Syphilis.

Some of the bone lesions of inherited syphilis may be congenital, whereas others develop during childhood and adolescence.

*Syphilitic osteochondritis or epiphysitis* is one of the commonest of the early lesions. It occurs usually during the first six months of life, and it affects especially the lower end of the femur, but also the tibia, the fibula, or the bones of the forearm. Often the affection is multiple



FIG. 45. Syphilitic osteitis of left parietal bone, from a child aged two and a half years.  
(Museum of Royal College of Surgeons of Edinburgh.)

and bilateral. Being painful, the lesions prevent free movement, and the limbs may appear to be paralysed (pseudo-paralysis of infancy).

*Gummata*, and *diffuse gummatous osteo-periostitis* may occur in

inherited syphilis. They have the same characters as in acquired syphilis, and tend to affect the same bones, especially the tibia and sternum. The tibia is liable especially to a diffuse osteoperiostitis, and as a result it becomes greatly thickened and sclerosed. Usually it becomes curved, with the convexity anteriorly, and is flattened from side to side, the so-called sabre tibia. Sometimes the sharpness of its margin is obscured and the bone may then resemble a cucumber in shape.

*Syphilitic dactylitis* is a form of osteoperiostitis affecting the metacarpals, metatarsals, or phalanges. The proximal phalanx of the index finger or thumb is most liable to the disease. New bone is formed under the periosteum, and a cylindrical, sclerotic enlargement results. Growth of the bone is interfered with and the digit may remain permanently short.

The cranial lesions of inherited syphilis are now recognized to be attributable to the malnutrition and debility associated with the disease more often than to a specific infection of the bone. Thus craniotabes, a condition of decalcification and thinning of the flat bones, particularly the occipital bone, is the result of malnutrition and is comparable to the cranial atrophy seen in rickets. "Parrot's nodes," the large bosses of spongy bone that form in the region of the frontal and parietal tuberosities, also have their counterparts in rickets. Erosions of the bones of the palate and nose, which result in perforations of the palate and in the characteristic depressed, saddle-shaped nasal ridge, are secondary results of combined septic and syphilitic lesions of the mucous membranes.

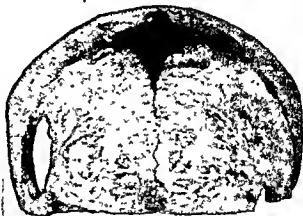


FIG. 49. Syphilitic osteitis of the frontal bone, from a child affected by inherited syphilis. The diploë and outer table are extensively destroyed, and in places the inner table is perforated. The ulcerative process is irregular in distribution, and gives a worm eaten appearance.

(Museum of Royal College of Surgeons of Edinburgh)

#### DIAPHYSIAL ACLASIS (Multiple Exostoses)

The term diaphysial aclasis has been applied by Keith to certain diseases characterized by disturbance of the growing ends of bones. The most notable example is the condition formerly known as *multiple exostoses*, but there is much evidence that the rarer *dyschondroplasia* should be included, as well as, perhaps, such conditions as *solitary exostoses* and *multiple chondromata*, which are usually classed as benign tumours.



Diaphysal aelasis usually occurs as a hereditary disease, and sometimes three or four generations are affected. The lesions are not recognizable at birth but appear in childhood. They are rarely very noticeable before the eighth or tenth year. Males are affected three times more commonly than females.

The disease is characterized by three associated pathological features, but all are not present in every case. The three features are (1) multiple irregular outgrowths of cartilage and bone, (2) failure of bone modelling at the ends of the diaphysis, (3) deficient growth in length of the long bones.

(1) The irregular outgrowths or exostoses constitute the most obvious feature of the disease. They are multiple and often in large numbers. They occur most frequently near the distal metaphysis of the femur and the proximal metaphysis of the tibia, but they may affect the humerus and other long bones, the scapula, the members of the pelvic girdle, and occasionally any other bone formed in cartilage. Exostoses of this type never arise from bones formed in membrane, and they never arise from epiphyses.

The exostoses are composed of unmodelled bone. Sometimes they are conical or pointed, sometimes rounded and globular. As a result of continued growth in length of the bone affected, the conical exostoses tend to point obliquely, away from the neighbouring epiphysis. Often one such conical projection lies at the junction of the normal and abnormal parts of the bone, whereas the globular projections usually are closer to the epiphyseal cartilage. An interesting feature of the disease is that the affected portion of bone is covered with a thin layer of cartilage from which growth proceeds. Ossification proceeds in this cartilage, and thus the exostoses and surface irregularities are formed. At about the age of twenty to twenty five, when



FIG. 50. Diaphysal aelasis. Posterior aspect of the right knee joint showing multiple exostoses arising from the metaphyses.

(Museum of Royal College of Surgeons of Edinburgh.)

growth normally ceases the cartilage ceases to form bone and becomes calcified. Not infrequently excessive growth of the cartilage leads to the formation of multiple chondromata, which are most common in the hands but may occur in many other situations.

(2) The failure of bone modelling when present is seen at the ends of the diaphyses and in these regions the bone is deficient in calcium and irregular in structure. Sometimes large rounded islands of cartilage

persist in the bones and are visible in radiograms as clear spaces in the bone shadow. The epiphyses are usually unaffected, but occasionally they are small, of irregular outline, and prematurely ossified.

(3) Deficient growth in length is a common accompaniment of diaphysal aclasis. The subjects of this disease are usually of less than average height, from premature cessation of growth of the long bones, and sometimes they are actually dwarfed. In some cases the paired bones in the forearm and leg grow unequally and this leads to deformities.

**The Nature of the Disease** The precise limitation of the lesions to the metaphyses of bones formed in cartilage indicates clearly that the fundamental feature of the disease is a disturbance of endochondral ossification, and that the disturbance does not occur in the early embryo but begins after the major portions of the bones have been normally formed. According to Keith, the essential factor is a failure of bone modelling, the process whereby normally bone newly formed at the metaphysis is remoulded and adapted to become a part of the shaft. The bone formed after the onset of the disease consequently remains unmodelled, with scanty Haversian systems irregularly disposed, and sometimes interspersed with masses of unaltered cartilage. The layer of cartilage on the surface, from whose deep aspect the growth of the exostoses proceeds, is believed to be derived from the epiphysal cartilage.

### DYSCHONDROPLASIA (Chondrodysplasia)

Dyschondroplasia was described by Olver in 1898 as a disease characterized by irregular ossification of long bones and by unilateral dwarfing. The term is now applied also to bilateral affections of similar character.

The disease may affect one bone, one limb or nearly every bone in the body. It generally becomes manifest in early childhood. The pathological changes are most marked in the metaphysal regions and do not affect the mid parts of the diaphyses. The bone may be somewhat broadened, and is occupied by masses of cartilage, which are traversed and divided by long trabeculae. Exostoses may be present, and multiple chondromata of the hands and feet have been observed.

The disease is now generally regarded as a variety of diaphysal aclasis, but differs from it in that a familial history is often lacking.

### FRAGILITY OF BONES

A bone owes its capacity for resisting stresses and strains to two inherent qualities, hardness and elasticity. Hardness of bone is obviously due to the mineral content, whereas elasticity depends upon the soft-tissue elements, the periosteum, the endosteum, the bone cells and fibres. Decalcification of bone leads to softening and pliability, whereas fragility or brittleness is due to affections of the connective tissue framework and may even occur when the mineral content remains normal. The bones may become fragile in rickets in infantile scurvy, or as a result of erosion by tumours, but the term "*fragility of bones*"

is usually restricted to certain congenital or inherited diseases of which fragility forms the predominating characteristic

Fragility of bone may be present in foetal life, or may become manifest in childhood, and for convenience of description it is preferable to recognize two distinct types, *osteogenesis imperfecta*, in which the fragility is evident at birth or in infancy, and "*familial fragility with blue sclerae*," which appears in later childhood

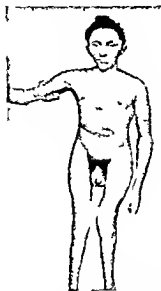


FIG 51 Familial fragility of bone. The man aged 21 years is dwarfed and shows the characteristic deformity of the head. The femora are deformed the result of old fractures and a marked degree of coxa vara is present. Blueness of the sclerae was present, but not marked

**Osteogenesis Imperfecta** The subjects of this disease are usually still born, but occasionally they survive and may attain adult life. The bones are excessively brittle, and break under the least strain, or even as a result of muscular action. Fractures are sometimes present at birth, and during infancy as many as a hundred may occur, and cause much deformity and shortening of the limbs. Union of the fractures is usually rapid, and sometimes is accompanied by excessive formation of callus. Apart from being fragile the bones may show little departure from normal. They are well calcified, though usually of slender build. Microscopically, there is sometimes evidence of a deficiency in the connective tissue cells of the bone, with irregularity in the disposition of the bone lamellae.

The long bones of the extremities are particularly liable to fracture, but no bone is exempt. The cranium often presents a curious deformity. It is of relatively large size, and very broad across the temporal regions. Sometimes there is an angular projection above the level of the zygoma, and the upper parts of the auricles may be projected laterally and thus rendered un-

duly prominent. Infants affected with *osteogenesis imperfecta* are usually born of normal parents and there is rarely evidence of an hereditary tendency. Death usually occurs at an early age from intercurrent disease, but if adolescence is reached the liability to fractures diminishes.

**Familial Fragility** This is an hereditary disease, which is transmitted in accordance with Mendelian laws as a dominant characteristic. It affects both sexes, and never "skips" a generation.

The fragility is usually, though not invariably, accompanied by other affections, of which the most obvious are blueness of the sclerae, abnormal laxity of ligaments, and a tendency to early deafness. According to Voorhoeve, all these affections are manifestations of an underlying hereditary hypoplasia of the mesenchyme.

Fractures do not usually occur before the second or third year

They do not occur so readily as in *osteogenesis imperfecta*, nor are they so numerous, and in most cases not more than six or eight occur. The fractures heal readily with well calcified callus. Fractures are rare after the age of sixteen or seventeen years. At this time the bones tend to become sclerosed, and in a few cases this process proceeds to an abnormal degree.

Blueness of the sclera usually accompanies familial bone fragility, but is not limited to that disease. The colour varies in depth from a dark greyish blue to "china blue," and it is most evident immediately outside the cornea. It is due to abnormal translucency of the sclera, which allows the pigment of the subjacent uvea and veins to show through. Abnormal laxity of ligaments is sometimes present and predisposes to sprains and dislocations. Lastly, many of the subjects of this disease are liable to otosclerosis, which comes on in early adult life and is steadily progressive.

### OSTEOPETROSIS (Marble Bones Albers-Schönberg Disease)

This rare disease, which may be familial, affects one or more bones, and is most commonly seen at the base of the skull in one of the vertebral bodies, or in a long bone. The affected bone presents areas of



FIG 5<sup>o</sup> Osteopetrosis, similar changes were present throughout the skeleton

greatly increased density, which render it very evident on radiography. The compact bone is involved first, and later the sclerosis encroaches on the marrow cavity, almost obliterating it. The remainder of the skeleton may be normal or show a certain amount of widespread osteoporosis. In a few cases there is an evident disturbance of calcium metabolism, and there may be calcium deposits in the kidneys or the soft tissues generally.

The term "marble bones" is a misnomer. "Chalky bones" would be preferable, for the affected bones though sclerotic are friable, and a pathological fracture is a common complication.

*Osteopetiolity* (speckled bones) is an affection of a kindred nature, characterized by the development of multiple small rounded foci of dense sclerosis, lying within the substance of bones which in other respects appear healthy (Fig. 52).

### ACHONDROPLASIA (*Chondrodystrophia Fœtalis*)

This disease, which arises in intra-uterine life, is characterized by disturbance of the normal process of endochondral ossification, which leads to dwarfing and to certain familiar deformities. The growth disturbance is believed to occur between the third and the sixth month of foetal life, and its effects are limited chiefly to those parts of the skeleton in which endochondral ossification is in progress. Sometimes the disease is inherited, and often affects several members of a family.

The subject of achondroplasia is rarely more than 4 feet 6 inches in height, but the trunk is well developed, and the dwarfing is due almost entirely to shortness of the extremities. Both upper and lower extremities are short, and contrast grotesquely with the trunk. The arms are so short that the finger tips may not reach the trochanters.

The long bones are especially affected. They are sometimes little more than two-thirds the normal length, but they are broad and well calcified. The epiphyses are always enlarged, sometimes greatly so, and may be of irregular shape. Fusion of the epiphyses with the diaphyses may be premature, but often it is delayed, and may even fail to occur.

Microscopic examination usually shows that the epiphyseal cartilage is narrow and the zone of proliferation is absent, and instead of the usual clumps of cartilage cells there are small groups of cells separated by intercellular substance. Fibrous tissue, cysts, mucoid areas and dense bone may be observed in various combinations. For this reason there is arrest of the normal growth in length of the long bones which remain of more or less equal size; the epiphyses grow normally, and are therefore proportionately greater in size than the diaphyses. Often the bones are bent in an exaggeration of the normal curves, and for this reason knock knee is common.

The head is large, rounded and brachycephalic, with prominent frontal and parietal eminences, and the nose is characteristically short, flattened and depressed at the base. These deformities of the skull result from failure of development of the cartilage-formed bones at the base of the skull. Failure of growth of the base of the skull limits the space available for accommodation of the base of the brain, but this is

compensated by an exaggerated growth of the membrane bones of the calvaria. The vertebral column may assume a deformity of lordosis, and the pelvis is usually narrowed in all its diameters. For this reason the pregnant achondroplastic is rarely delivered of a living child except by hysterotomy. The hands have a characteristic appearance, being short and broad, and the fingers are of almost equal length (trident hand). Delayed ossification is often apparent in the carpal bones, so that an achondroplastic child of ten or twelve years may have the carpal ossification normal for a child of one year. Achondroplastic dwarfs are readily distinguishable from cretins and mongoloid imbeciles on account of their muscular and intellectual vigour. Moreover, their sexual development is normal, or sometimes precocious.

### OSTEOCHONDRITIS JUVENILIS

The term osteochondritis is used to denote a variety of conditions, described during the last few decades, which occur during childhood or adolescence and affect the epiphyses. The most familiar examples are those at the hip, the tibial tuberosity, the calcaneum, the tarsal navicular, and the vertebrae, but the disease is also known to occur in almost a score of other situations.

It is now generally believed that all these various lesions are but manifestations of some common fundamental process, modified in different situations by local factors. The lesions occur at a definite age period, which is determined by the time of appearance and fusion of the affected epiphysis, and they occur in epiphyses particularly subject to undue stresses and strain. Usually only one site is affected, but in a few cases more than one lesion has been observed.

The conditions have much in common. They occur more frequently in boys than in girls, and often follow slight trauma. The course of the lesion is characterized by a short active period, followed by resolution. Symptoms are usually mild and may sometimes be absent, in great contrast to this, the radiological features are always arresting.

**Osteochondritis of the Hip (Legge Calvé-Perthes).** This is a disease of childhood and occurs most often between the ages of five and nine years. It is characterized by the signs of a fleeting synovitis and by a sequence of osseous changes which are out of all proportion to the mildness of the disability.

The first sign is usually a lump insidious in origin and with or without pain either at the hip or referred to the knee. A variable active period, sometimes with a mild pyrexia, is followed by gradual resolution. The joint usually presents only slight limitation of the movements of abduction and medial rotation. Within these limits movement causes no pain, and there is rarely muscle rigidity or atrophy.

Radiographic examination shows that the disease affects the head and neck of the femur, and to a less extent the acetabulum.

In the femoral head the first change is a slight flattening of the epiphysis. Then the most characteristic change develops, an appearance of "fragmentation" of the bony nucleus of the epiphysis into a number

of bony islands interspersed with zones of osteoporosis. Presently the head becomes more flattened, and its margins everted out mushroom fashion beyond the rim of the acetabulum. At this stage the flattened deformed, "fragmented" head gives a striking radiographic appearance out of keeping with the mildness of the arthritis. Later still, when the healing stage sets in, the deformed areas disappear, the bony islands coalesce and the bone resumes its normal density and trabeculation.

The flattening deformity may remain, and even increase and lead to chronic arthritis.

In the neck of the femur the same cycle of osseous changes leads to softening of the bone, to broadening and shortening of the neck and to a degree of *coxa vara*. In the acetabulum the same changes may occur, leading to the adaptation of its articular surface to the altered shape of the head.

Histological and bacteriological investigations of the disease have been either unhelpful or misleading. On exposure of the joint the synovial membrane has sometimes been found normal, in other cases a mild synovitis has been present and the joint has contained



FIG. 51. Osteochondritis of hip (Legg-Calve-Perthes). The femoral head shows the fragmentation and deformation characteristic of this disease.

a slightly turbid, straw-coloured fluid. In a case reported by Perthes histological examination of the epiphysis displayed what he regarded as a non-inflammatory replacement of cancellous bone by invading buds of cartilage. Phemister on the other hand, described a case which, he considered, gave evidence of an old infective lesion, probably from an avirulent pyogenic organism.

Many theories have been advanced to account for the condition. It is now definitely recognized that tuberculosis, syphilis and rickets can be excluded, and there is no evidence that the disease owes its origin to endocrine derangement. At present two views hold the field (a) that the disease is a low-grade inflammatory lesion, from avirulent organisms, and (b) that the essential factor is trauma either a single injury or perhaps repeated stresses and strains, followed by alterations in the blood supply to the area affected. This latter view is supported by the age and sex incidence of the disease, and by the history so commonly obtained of some definite though minor injury.

**Tibial Apophysitis (Osgood, Schlatter)** This is an osteochondritis affecting the tibial tuberosity, and it usually affects boys between the ages of twelve and sixteen years. It is essentially traumatic, a partial separation of the tuberosity as the result of sudden or excessive traction exerted through the fibres of the patellar tendon, or of a direct contusion. The affection gives rise to mild discomfort and local swelling over the tubercle. Radiographically, the changes are similar to those at the hip. The bony nucleus of the apophysis is fragmented, and later becomes increasingly dense in a patchy manner. Its surface becomes irregular, and there is either a real or an apparent increase in the space between the apophysis and the diaphysis.

In the majority of subjects the tuberosity of the tibia develops as a tongue like projection from the anterior part of the proximal tibial epiphysis, but in a proportion of cases the apophysis grows from a separate centre, which appears at the age of eleven years and usually fuses with the remainder of the epiphysis at from twelve to thirteen years. It has been suggested that osteochondritis is more prone to develop in those in whom this independent development occurs.

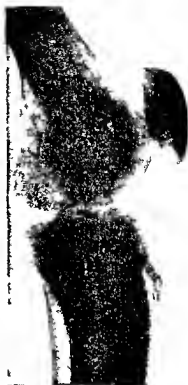


FIG 54 Tibial apophysitis

**Osteochondritis of the Tarsal Navicular (Köhler)** This condition occurs in younger children, between the ages of three and eight years. It has an insidious onset, with slight pain on walking, a limp, and some pain and tenderness over the bone. An active period of variable duration is followed by resolution.

The characteristic radiographic picture shows a navicular smaller than its fellow, and of irregular outline. The bone is increased in density, is flattened from before backwards, and the normal architecture is lost.

The condition is usually regarded as the result of a mild inflammation. Clinically and radiographically in its early stages it is not unlike tuberculosis and immediate differentiation may not be possible.

**Epiphysitis of the Calcaneum (Sever)** This is a condition met with in adolescents, usually boys, between the ages of ten and thirteen, affecting the posterior epiphysis of the calcaneum. There are pain and limping of variable duration associated with difficulty in putting the heel to the ground. On radiographic examination, the same changes described in analogous affections elsewhere are noted. The calcaneal epiphysis appears narrow and irregular, with great increase in bony



and its severity is out of proportion to the nature of the crural injury it is aggravated by movement and is not relieved by immobilization. Stiffness and loss of function are probably the outcome of pain and associated muscle spasm. The vasomotor phenomena are of special interest: the part remains cold, and for long retains a dusky cyanotic tinge and the skin is glossy and the subcutaneous tissues œdematous.

The ætiology of this variety of osteodystrophy does not admit of

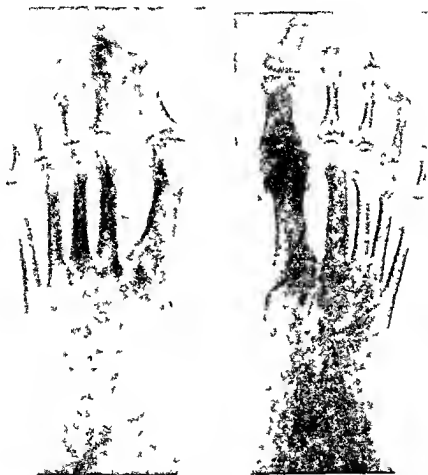


FIG. 53. Radiographic appearances of post traumatic osteodystrophy affecting the bones of the foot: a film of a normal foot (right) is for comparison. The osteoporosis involves the tarsal bones and the extremities of the metatarsals: the shafts of the metatarsal bones are little affected.

ready explanation. The decalcification suggests that hyperæmia has been prolonged and exaggerated. So far as can be deduced the initial trauma promotes an abnormal reflex in the autonomic innervation of the part, whereby afferent pain bearing impulses are transmitted to reflex centres which, in turn, convey vasomotor and other stimuli, resulting in sustained vasodilatation peripherally—possibly the result of excessive production of histamine locally. Probably a vicious circle is established: local hyperæmia keeps up pain and the pain (reflexly) maintains hyperæmia. The benefit which may follow sympathetic

denervation of the part, though logically it might be expected to exaggerate hyperæmia, probably owes its effects to the abolition of the excitatory influences of painful stimuli from the injured part

### POST-TRAUMATIC SPONDYLITIS (Kummell, Verneuil)

This affection was mentioned by Verneuil in 1892 and described in more detail by Kummell in 1894. It is a delayed sequel to injury of the spine, and it is characterized by progressive decalcification of a single vertebral body, with consequent collapse of the body and the production of a kyphosis. The condition is almost limited to the male sex and it is commonest in early adult life, though not unknown either in childhood or in middle age.

The initial injury is a forcible flexion of the spine, such as may cause compression of the vertebral bodies. It usually arises from the impact of heavy weights upon the bent shoulders, as in pit accidents, the force being transmitted through the concavity of the spinal column and exercising its compressive effect upon the lower thoracic or upper lumbar vertebrae. In other cases the injury results from falls from a height, the force being then transmitted upwards from the feet or buttocks and exercising the same effect upon the spine. The initial injury is not necessarily a severe one, and the dystrophy has been known to follow such trivial accidents as arise from jumping from a slowly moving vehicle.

In most cases at the time of injury there is clear evidence of damage to the affected vertebrae, a compression

fracture of minor degree, and sometimes there is a temporary paraplegia or other evidence of cord involvement. In others the immediate symptoms are mild and transitory. The closest scrutiny may fail to reveal actual fracture, but some degree of injury to the vertebra must be presumed.

Following the injury there is an interval of several months or even years during which subjective symptoms and signs are absent. The dystrophy becomes manifest subsequently, and attention is usually drawn to it by pain, with weakness of the lower limbs and eventually, in some cases, progressive paresis culminating in paraplegia. Examination carried out at this time reveals a striking deviation from the



FIG. 56. Post traumatic spondylitis. Extreme decalcification of the first lumbar vertebra, with subsequent collapse of the spine and an angular kyphosis. In this case the affection was a late sequel to a fall from a ladder.

normal. An angular kyphosis is usually present, and radiological investigation shows that this is the result of collapse of the affected vertebral body, which is decalcified to an extreme degree.

The fundamental feature of the disease is a post traumatic decalcification, and there is much to suggest that the affection is similar to the decalcification which follows injuries to the carpal lunate or other bones. It has been suggested that the vertebral dystrophy is the result of a trophic disturbance following injury to the nerves of the affected vertebra, but it seems more probable that the fundamental factor is disturbance of the nutrition of the bone.

### POST-TRAUMATIC CARPAL DYSTROPHY

In 1910, Kienbock described the affection of the carpal lunate bone now generally known by his name, a late sequel of injury to the bone which is characterized by alteration in its structure with irregular patchy decalcification and subsequent sclerosis. Since then similar affections have been observed though less commonly, in the navicular and other bones of the carpus and in the metacarpus.

The dystrophy of the lunate bone, being, at least in the great majority of cases, a result of injury, is naturally commoner in males than in females, the proportion being about seven to one. For the same reason it is fully twice as common in the right as in the left wrist. The injury may be either a sudden severe blow, such as may be occasioned by a fall on the outstretched hand or repeated minor injuries. In some cases there has been a suspicion that the initial injury amounted to an unrecognised fracture or a momentary, spontaneously reduced, dislocation.

The dystrophy does not immediately succeed the injury, but becomes apparent after an interval of several weeks or months, during which the disabling effects of the injury may have subsided. The dystrophy manifests itself in a recurrence of the disability, with fixation of the wrist, swelling over the dorsal aspect, and pain either on pressure or on movement. From diminution in the size of the lunate bone this metacarpal may attain an unduly proximal position in the hand, with diminution of prominence of the metacarpal head.

Radiological examination reveals a characteristic change in the form and structure of the lunate. The bone is narrowed, and in place of the normal uniformity there is an irregular, patchy increase in the density of the bone shadow. In some cases the denser patches are interspersed by areas of diminished density and may simulate fracture. In addition, osteoarthritic changes may ensue.

The cause of the dystrophy is not yet clearly established. Kienbock attributed it to rupture of blood vessels caused by momentary dislocation of the bone, but such a gross injury can only be responsible in a small proportion. In some cases it seems rational to presume that the dystrophy results from some less obvious interference with the vascularity of the bone.

### METATARSAL DYSTROPHIES

The forefoot has undergone fundamental changes during the evolution of orthograde man from his primitive arboreal stock, in order to

render the foot able to take the body weight during standing and walking. It seems likely that an atavistic structural anomaly of the forefoot by predisposing to strain may be a factor in the ætiology of a number of diseases characterized by metatarsal pain. In a recent paper Bruce has put forward evidence for including such widely differing conditions as metatarsalgia (Morton's Disease), marching foot (Deutschlander's Disease) and the Kohler-Freiberg disease of the metatarsals in this single group.

**The Primary Anomaly.** In the pronograde foot of apes, adapted for prehension the hallux is thumb-like with a short metatarsal bone widely abducted in the varus position and very mobile in relation to the other metatarsal bones. During evolution towards the human form the hallux metatarsal becomes adducted towards the other toes, it becomes fixed in position and its length approximates more closely to that of the other metatarsals. Coincidentally it becomes thickened and strengthened and assumes an important part in the formation of the longitudinal arch of the foot.

Quite commonly the first metatarsal bone presents a structural anomaly which may be regarded as an atavism: the bone is abducted to the varus position, is relatively short and possesses an exaggerated mobility (*metatarsus varus brevis et mobilis*). This anomaly tends to weaken the longitudinal arch of the foot. The weakness may be compensated by bony hypertrophy or by an increase in muscle tone (especially of the adductor-hallucis muscle which serves to anchor the first metatarsal bone to the second, and the lumbricals and interossei which keep the small toes in contact with the ground and so diminish the load on the metatarsal heads). If however these compensatory mechanisms fail as may occur from strain, overwork, illness or malnutrition, an increased strain is placed upon the forefoot and one or more of the following affections may develop. All of them are characterized by pain in the ball of the foot, swelling over the dorsum of the metatarsal region, dorsiflexion of the metatarso-phalangeal joints and pain on moving the toes.

**Metatarsalgia (Morton's Disease).** Two varieties of metatarsal pain are included under this term. The one which is of neuralgic character has been attributed variously to compression of a digital nerve between the contiguous heads of the metatarsal bones or to traumatic inflammation of a small adventitious bursa sometimes found in this same situation. The other which is of a constant, aching character and situated under the ball of the toes is attributed to a strain of the metatarsal arch.

**Marching Foot (Deutschlander's Disease).** This very disabling condition occurs mainly in infantry recruits or in bikers and comes on after unusually strenuous marching. It has also occurred in those such as nurses whose occupation entails much standing. The disease affects one of the metatarsal bones usually the second one and it is characterized by the development of a mass of bone in relation to the middle of the metatarsal shaft. In most cases the metatarsal shaft presents a fracture at this level. Recent radiographic investigations indicate that the earliest feature is the formation of new bone under the periosteum

around the shaft, and that later the shaft becomes decalcified and eventually undergoes fracture. It is thought that the essential ætiological factor is a bending strain imposed upon the delicate metatarsals in walking, as a result of strain of the forefoot induced by a metatarsus varus deformity.

**Kohler-Freiberg Disease of the Metatarsal Heads.** This affection, which must be distinguished from Kolder's disease of the tarsal navicular, is characterized by decalcification and collapse of the spongy bone immediately subjacent to the articular cartilage on the dorsal aspect of the head of one of the metatarsals, generally the second. The affected bone may form a loose fragment and be set free in the proximal toe joint. A hammer-toe deformity is often present, and it has been suggested that minor trauma acting along the line of the first phalanx constitutes an ætiological factor, superimposed upon the strains associated with a decompensated metatarsus varus.

**Dystrophic (Fatigue) Fracture.** Bone changes similar to the above have been observed in the long bones, especially in the upper third of the tibia and the distal end of the fibula. In the tibia the change is marked by a zone of rarefaction in the shaft of the bone some 2 to 3 inches from the epiphysis, with a variable amount of new bone formation at the same level on the outer, less often the inner, aspect of the tibia. In rare instances, if untreated, it culminates in complete fracture.

The origin of the dystrophy, which has received the title of "fatigue fracture," is a matter of conjecture. It is believed to result from prolonged stress at the affected part of the bone.

## RICKETS

The word "rickets" is probably derived from the Old English "wricklen" ("to twist"), and it describes well the skeletal deformities characteristic of the disease. From the surgeon's point of view, rickets is sometimes regarded as entirely a disease of bones, but actually the bone lesions form only one aspect of a constitutional disorder that affects almost every system of the body, and the early symptoms are more often related to the gastro intestinal tract or the general health than to the bones.

Rickets is now known to be due to deprivation of vitamin D. In Great Britain formerly it was common among children of the poorer classes, whose diet was deficient, and especially in the large towns where the ultra violet rays of sunlight are filtered off by the smoke pall. Since about 1917, when cod liver oil and other vitamin rich preparations came into general use for infant feeding, the disease in its active form has almost disappeared, though "sub clinical" types are common.

Rickets begins usually between the ages of six months and two years. After a variable period, a few months or a year or so, the active phase may cease, but its effects upon the skeleton remain, either as obvious deformities of the extremities, thorax and skull, or as less obvious deformities of the pelvis.

In the active phase of the disease the child is anæmic and wasted. There is a general enlargement of lymph glands and of the spleen,

and this, with much muscular hypotonicity, causes the characteristic protuberant "pot belly." Often there are recurring attacks of bronchitis and of diarrhoea, and there may be such nervous symptoms as tetany or convulsions.

**Changes in the Bones** The rôle of vitamin D is to facilitate the absorption of fats from the alimentary tract and thus to promote



FIG. 57 Active rickets in a young child. Radiograph showing broadening and irregularity of the metaphyses.



FIG. 58 Rickets affecting knee region. Radiograph showing broadening and irregularity of metaphysical regions and secondary bowing of femur.

absorption of calcium phosphate. When it is lacking, osteogenesis is impaired. Thus there is a temporary disturbance of the ossifying process whereby the bone that is formed during the active phase of the disease is disposed very irregularly and is soft, pliable and readily deformed. The bone formed before the onset of the disease is less affected, after the disease has run its course the normal process of bone formation is resumed, but that part of the bone laid down during the florid stage of the disease for long remains obvious.

If a longitudinal cut be made at the end of a healthy growing bone

the site of growth is represented by a thin white transverse line, which marks the orderly replacement of cartilage by bone. In rickets the appearance is very different. In place of the thin white calcified line there is a broad pale yellow area, soft and devoid of calcium. In this broad strip the ossifying process is totally disordered, and irregular islets of unchanged cartilage alternate with areas of imperfectly formed bone. In addition, the whole region of ossification is expanded laterally and swollen, and under the stresses of weight bearing or muscular activity the softened bone often becomes bent or curved. Deformities are a natural sequel.

*At the costochondral junctions there develop raised bead like nodules*

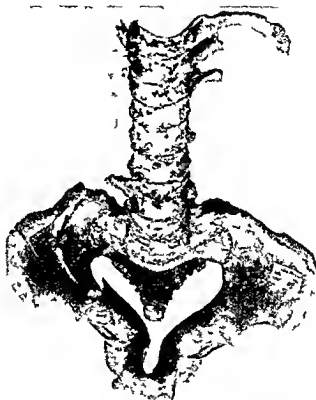


FIG. 59. Rickets deformity of the pelvis. The pelvic bones are beaked anteriorly, the acetabula are displaced medially and the pelvic aperture has assumed a trefoil shape. The sacrum has rotated under the body weight and the promontory is projected anteriorly.

(Museum of Royal College of Surgeons of Edinburgh.)

which project both superficially under the skin and deeply towards the thoracic cavity, the rickets rosary. A "pigeon breast" deformity sometimes results from bending or infraction of the ribs from the stresses of respiratory movements, and a horizontal sulcus (Harrison's sulcus) may appear, from traction on the soft ribs.

The long bones in rickets are often bent, especially in children who are not too feeble to crawl or walk. In the femur the natural curves are exaggerated and the bone is bowed both forwards and laterally. Yielding of the femoral neck under the body weight may lead to a severe degree

of coxa vara. The tibia is often bent both anteriorly and laterally, and a pronounced degree of bow leg may result. Occasionally the reverse deformity, knock knee, occurs, and rarely one limb is bent inwards, the other out. The growing ends of the long bones become swollen. This is often obvious at the distal ends of the radius and tibia particularly if the child has been allowed to support its weight on these bones.

The pelvis, which is subject to so many stresses from adoption of the upright position may be greatly deformed if the child is allowed to stand. Two principal types of deformity are recognized. Most often there is flattening of the whole pelvis with diminution in the conjugate diameter. rarely the pelvis assumes a trefoil shape as in osteomalacia. Either of these deformities may later be an impediment to parturition.

The skull becomes broadened, from the formation of much soft

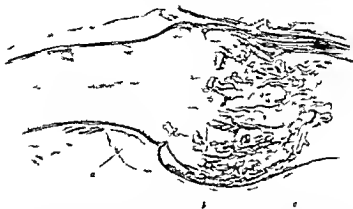


FIG. 60. Endochondral ossification in rickets. A microscopic section of the costochondral junction of a rickety puppy (low power). (a) Pre-formed hyaline cartilage. (b) Zone of proliferation of cartilage cells. (c) Newly formed bone trabeculae. The whole region of ossification is enlarged and deformed. The cartilage cells have proliferated irregularly and persist in islands among the bone trabeculae. The trabeculae are almost devoid of calcium.

osteoid tissue under the pericranium. The forehead is square and broad, and large bosses develop over the frontal and parietal tuberosities. The vertebral column is affected (hence the name *rachitis* which is sometimes applied to the disease) and from softening of the bones and laxity of the soft parts there develops either kyphosis or, more often, scoliosis. Lastly, dentition is delayed, and calcification of the teeth is defective.

**Microscopic Appearances.** Rickets affects principally those parts of the bones that are actively growing, and the process is therefore most obvious near the ends of long bones, to a less extent it is seen also under the periosteum.

The microscopic changes characteristic of the process of endochondral ossification have already been described (see p. 112).

The process in rickets is very different, for here all is disorder. The cartilage cells proliferate, sometimes to excess, but instead of forming straight columns they lie in irregular masses, the zone of



provisional calcification is no longer a thin well defined white line, but is uneven and indistinct, the invading capillaries run in all directions, the bone cells proliferate irregularly, and, since no calcium is available, only imperfectly calcified osteoid tissue is produced. Large islets of hyaline cartilage remain altogether unaltered, and may persist in regions normally occupied by fully formed bone.

When the disease has run its course the first evidence of healing is the deposition of calcium, first as a thin irregular line of poor density, later in greater amount. That portion of the bone formed during the rickety period remains for a long time imperfectly calcified. Eventually, however, it heals, leaving little abnormality.

Radiographic studies afford confirmatory evidence of each phase of the disturbance of ossification. If there has been no weight bearing there is an unusual broad belt of translucent uncalcified osteoid tissue between the epiphyseal plate and the diaphysis. The epiphyseal itself is blurred and irregular. Later, when there has been weight bearing the soft and redundant bone yields to pressure and the epiphyseal line becomes even more irregular, the end of the bone is broadened, and as calcium is more deficient in the central axis of the bone a scooped out or cup shaped appearance results.

### OSTEOMALACIA

In virtue of its derivation (*ὀστέον*, bone, *μαλακός*, soft), the term osteomalacia may be applied correctly to any condition of bone softening, but it is now by custom limited to one special type of affection. This is a generalized skeletal disease which almost always affects pregnant or parous women, especially women debilitated by inadequate food, restricted freedom, frequent pregnancies and prolonged lactation. Very occasionally men are affected (senile osteoporosis). A similar condition, "hunger osteomalacia," was prevalent in the starving population of Vienna during 1919-20, especially in middle aged subjects of both sexes.

The disease is characterized by extreme decalcification of the bones, with consequent deformities from curvature or fracture. It usually commences during pregnancy and undergoes remission at the termination of lactation, but the progress is greatly hastened by succeeding pregnancies and a fatal outcome is rarely delayed more than a few years.

The cause of osteomalacia is not yet definitely determined and indeed it seems likely that there is no one cause, but a number of contributory factors. In the later months of pregnancy a large amount of calcium is required for foetal ossification, during lactation a large amount is lost in the milk, and when for any reason intake of calcium is inadequate the deficit is made good at the expense of the skeleton.

Thus the underlying causative factor in osteomalacia appears to be a deficient intake of calcium. This may result either from a faulty dietary or, more often, from impaired absorption in the intestinal tract, as in idiopathic steatorrhoea. There is evidence that in many cases impaired absorption results from a lack of vitamin D and osteomalacia is thus comparable to rickets.

Osteomalacia in gross form is rare in Great Britain and America,

but it is not uncommon in parts of France Austria and Italy, and it is endemic over wide areas of Northern China and Northern India. The reasons for this distribution are not far to seek. In the north of China the diet is often deficient in calcium and in vitamins, and the severity of the winter and the practice of foot binding combine to keep the women indoors. In India the observation of strict purdah entails close confinement, and the risk of cholera prevents the free use of fresh

vegetables and fruits. Both in China and in India prolonged lactation is customary, and this results in great depletion of the calcium reserves.

#### Appearance of the Bones

The bones are decalcified to an extreme degree, and as a result they are soft, pliable, and readily cut with a knife. In some cases they may be bent or twisted with ease. On section it is seen that the bone is extremely porous. The trabeculae are eroded, and sometimes little osseous tissue remains except in the cortex. The marrow and all the interstices of the bone are filled with connective tissue of great vascularity.

Microscopic examination confirms the changes just described. The enlarged lacunae of the bone contain numerous large blood vessels with young fibrous tissue and the bone trabeculae are narrowed or almost obliterated. A striking feature is the great paucity of calcium. The outer zones of the trabeculae are composed of

poor tissue completely lacking in calcium, and such calcium as of it is concentrated in small deposits at the centre of the trabeculae most. Deformities. Skeletal deformities constitute the most obvious under the osteomalacia. All parts of the skeleton participate, but the deformities are most evident in the parts of the bones exposed to the action of gravity or muscular action (so-called Looser's zones).

The proximal bones are especially affected. The acetabula are forced together by the pressure of the femoral heads, and the pubic bones forming straight anteriorly, the sacrum is rotated under the body weight.

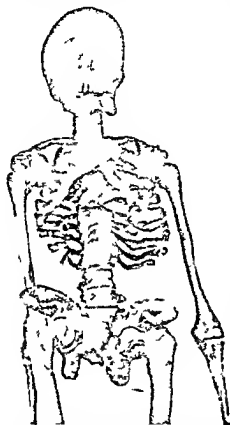


FIG. 61. Osteomalacia. The pelvis is greatly deformed and there is a bilateral costal deformity. The ribs and the sternum are distorted.

L. (Museum of Royal College of Surgeons of Edinburgh.)

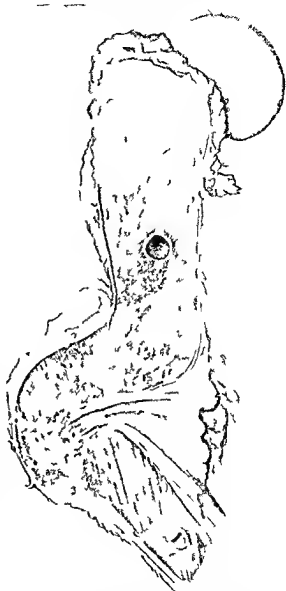
and its promontory is projected forwards, and thus the upper pelvic aperture assumes a trefoil shape (*see Fig 61*)

The bones of the lower extremity are usually deformed by weight bearing. The femur and tibia may become bowed with an antero lateral convexity and coxa vara develops. The ribs are bent medially in their mid portions, and the vertebrae may soften and collapse.

Death may be due to intercurrent pneumonia, or to complications during parturition, the result of the pelvic deformity.

### OSTEITIS FIBROSA (Fibrous Osteodystrophy)

Osteitis fibrosa may occur as a generalized disease affecting the whole or the greater part of the skeleton, or as a localized affection of a single bone. It may affect either sex, but is twice as common in women as in men. The generalized disease arises usually in early adult life, it runs a progressive course and it usually terminates fatally within a few years of the onset. The localized disease, on the other hand, usually commences in adolescence, and progresses slowly, and in some cases it may become stationary. In their pathological features moreover, the two types differ somewhat, and they will therefore be described separately. The generalized type is the less common, but owing to the extensiveness of its manifestations and the more frequent



**FIG 62** Osteitis fibrosa of the femur. The bone is extensively replaced by vascular connective tissue and contains two cysts. A pathological fracture has united in faulty position and the softened bone has become greatly deformed.

(Museum of Royal College of Surgeons of Edinburgh)

opportunities for post mortem investigation it has been studied much more minutely than the localized type

### Generalized Osteitis Fibrosa

This uncommon disease was first adequately described by v. Recklinghausen in 1891. It is characterized by wide-spread skeletal changes with decalcification and fibrosis of the bones and often by the formation of cysts and tumours. In the majority of cases the disease results from hypersecretion of the parathyroid glands, usually due to a tumour.

(1) *The Skeletal Changes* The outstanding pathological change in the bones is decalcification, and it may proceed to extreme degrees. The cancellous bone is principally affected, but the cortex also shares in the process.

As a consequence of the decalcification the bones are greatly softened and they are very liable to curvatures or fractures. Sometimes they are so soft as to be cut readily with a knife. The stresses caused by gravity and muscular action lead to gross deformities. The femora are bowed antero-laterally, coxa vara develops, the tibia

becomes convex anteriorly, the vertebral column becomes kyphotic, the ribs bend at their angles and produce a pigeon breast deformity, and the pelvis may assume the trefoil shape of osteomalacia.

The bones are increased in girth but smooth on the surface and covered by normal periosteum. Cortex and cancellous bone are extremely spongy and their interstices are filled with soft vascular granulation tissue which replaces the whole fatty marrow. Microscopically, the trabeculae and lamellae are lacking in calcium



FIG. 63. Osteitis fibrosa. The bone trabeculae are reduced in size and the intervening spaces are occupied by vascular fibrous tissue. There are numerous giant cells of osteoclast type mainly situated in apposition to the bone trabeculae.

(Laboratory of Royal College of Physicians of Edinburgh.)

and are greatly reduced in size. The lacunae, which are correspondingly enlarged, are filled by vascular young connective tissue in which are numerous multinucleated giant cells of 'osteoclast' type. In places there is evidence of the formation of new bone, which is almost devoid of calcium (osteoid tissue).

Cysts of various size, sometimes as large as a golf ball, are usually

present, probably as a result of degenerative changes. They contain brownish, watery fluid or gelatinous material. When large they render the bone very liable to fracture.

In many cases multiple tumours are also present in the affected bones. The tumours are solid or partly cystic, and of brownish or reddish colour, and microscopic examination shows that they have the characters of giant cell tumours (*see p 160*). The tumours are usually of small size, but one or more may enlarge and attain considerable dimensions. They usually pursue a non-malignant course, but occasionally they may undergo sarcomatous change. The tumours of osteitis fibrosa present one of the most interesting problems in the whole field of oncology, for they have all the characteristics of true neoplasms, yet are apparently an end result of the excessive output of parathyroid hormones.

(2) *Hyperparathyroidism in Osteitis Fibrosa* It is now recognized that in most cases the skeletal changes characteristic of osteitis fibrosa occur as a secondary result of over activity of the parathyroid glands. Generally, an adenoma of one of the parathyroid glands is responsible. The tumour may be in a normally placed gland or may be situated behind or in the thyroid gland, behind or in front of the oesophagus or in the mediastinum. It is often of small size, or may be as large as 7 cm in the long axis. Less often there is no tumour but a diffuse hyperplasia of one or more of the glands.

Hyperparathyroidism is believed to cause decalcification of the skeleton in virtue of its effect upon the inorganic phosphates of the blood. Its first effect is to cause excretion of phosphates and thus to reduce the ionic phosphate content of the blood. For the reasons discussed on p 113, this demands a corresponding increase in the ionic calcium of the blood, which is effected by liberation of calcium from the skeleton.

Thus while the bones become progressively rarefied, the calcium content of the blood is increased, from the normal figure of 10 mgm per cent to 12 mgm per cent, or even to over 20 mgm per cent. As a secondary result, calcium "overflows" into the urine, and the urinary calcium may be increased to eight times the normal amount. Often this leads to the formation of urinary stones. In a few cases the excess of calcium is deposited in certain tissues, notably the kidney and the stomach wall. The phosphate content of the blood is raised.

It should be mentioned that in a small proportion of cases osteitis



FIG 64 *Osteitis fibrosa cystica*. The shaft of the femur is broadened and decalcified. The cortex is thin and the distinction between cortex and medulla is lost.

(By courtesy of Dr Scott Park.)

fibrosa cannot definitely be attributed to hyperparathyroidism and is of unknown etiology. For this reason, parathyroidectomy should only be advised if there is definite evidence of hyperparathyroidism. In most cases increase in the calcium content with diminution in the inorganic phosphate content of the blood puts the matter beyond doubt. There have been, however, a few recorded examples of undoubted parathyroid osteitis in which such abnormalities could not be detected, and in which an increase in the calcium content of the urine was the only evident biochemical abnormality. Even this may be absent in patients with anorexia owing to deficient intake of vitamin D.

### Localized Osteitis Fibrosa

This affection is considerably more common than the generalized disease and it differs greatly in its course. It arises usually in adolescence, progresses slowly over a period of several years and often undergoes remission. A single bone is usually affected or rarely two or three bones. The upper end of the femur is the commonest site, less often the humerus or tibia, but no bone is immune. The first part of the bone to be affected is the metaphysis and from here the disease spreads down the shaft. It rarely involves more than half the length of the shaft and the epiphysis usually remains free. Cysts of various

size are usually present, and occasionally almost the whole affected area is replaced by a single large cyst (one type of simple bone cyst).

The cysts render the bone very liable to fracture, but in spite of the lack of available calcium the fracture may heal with firm bony union, though slowly. The stimulus of the fracture may lead to arrest of the disease.

Localized osteitis fibrosa differs from the generalized form in that it has no evident relation to parathyroid disorders or to disturbances of calcium metabolism. Parathyroid overgrowths have not been observed, the blood calcium is normal and there is no disturbance of the calcium balance.

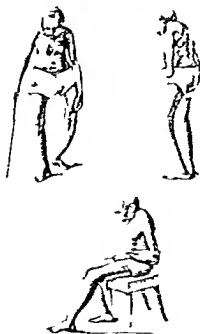


FIG. 60. Osteitis deformans. Paget's original case. A man aged sixty-eight years who had suffered from pains in the limbs during twenty-two years. Eventually a sarcoma of the radius developed. Note the curvatures of the vertebral column and lower limbs and the large size of the head. (After Paget.)

### OSTEITIS DEFORMANS (Paget's Disease)

In 1876, Paget described a generalized affection of the skeleton occurring in middle-

aged or elderly subjects of either sex and characterized at first by decalcification of the bones with softening and curvature, and sub-



FIG 66 Osteitis deformans The calvarium from Paget's original case  
Note the great increase in the thickness and density of the bone  
(After Paget)

sequently by recalcification and hardening of the bones. Every bone is affected to a greater or less degree, but the principal changes are generally seen in the bones of the lower extremity, the skull, spine, and clavicles. A similar disease sometimes occurs which involves a single bone or a few related bones, the remainder of the skeleton being unaffected.

The affected bones are increased in thickness, and, becoming softened, undergo deformation. The tibia becomes convex anteriorly, the femur bows forwards and laterally, coxa vara develops, and the patient becomes broad hipped, bow legged and bent.

The surface of the bone in its final stage is rough and deeply furrowed, and extensively pitted. The periosteum does not appear to take part in the disease and is not thickened, but it is often firmly adherent to the underlying bone.

On longitudinal section the most striking feature is a loss of the normal distinction between compact and cancellous bone. At first the whole bone is spongy, and both the bone spaces and the marrow cavity are filled with vascular connective tissue. Later, as the vascularity subsides the texture becomes more solid, and the bone is "more compact looking, and dense like limestone" (Paget). Finally, near the surface the bone may assume an ivory like sclerosis, but this is a rare change and is limited to small areas. Small cysts containing yellow or reddish gelatinous material may occur.



FIG 67 Osteitis deformans The femur from Paget's original case  
Note the coxa vara deformity, and the great increase in thickness and density of the bone  
(After Paget)

The skull is always affected in some degree. The disease involves the cranium principally, and the bones of the face are but little affected. The base of the skull sometimes participates but may escape. The bones of the vault show an increase in thickness, sometimes to as much as 2 cm. Such enlargement is responsible for one of the first signs of the disease, a progressive increase in cranial circumference. The increase in thickness does not cause the cranial cavity to be reduced in size but sometimes the frontal air sinuses are encroached upon. The diploe of the flat bones is narrowed or even obliterated. The bone is at first soft and vascular, and in the macerated specimen the sponginess is so great that water poured into the calvaria flows readily to the exterior. Later the bone becomes dense and hard.

In the vertebral column similar pathological changes occur, and from the generalized softening the whole column becomes shortened and bent. A regular anterior concavity of the whole spine commonly develops. The vertebral changes, together with deformities of the femora and tibiae bring about progressive diminution in stature, even to the extent of a foot. A further result of the vertebral changes is a narrowing of the vertebral canal, and in rare cases this may lead to compression paraplegia.

In the upper limbs, the clavicle, humerus and ulna are the bones most obviously affected. The clavicle becomes thick, and an exaggeration of its normal curves leads to undue prominence. The humerus and ulna may become curved with a posterior convexity. With the bending of the trunk and lower limbs there is a relative elongation of the upper limbs, and the attitude of the patient may finally bear a striking resemblance to that of an anthropoid ape.

**Microscopic Appearances** The microscopic appearance of osteitis deformans varies at different stages of the disease. At an early stage decalcification predominates, and the thickness of the lamellæ is decreased. The bone lacunæ are enlarged and filled with vascular connective tissue, which often contains giant cells of "osteoclast" type. At a later stage new bone formation is seen. The new bone is formed on an irregular pattern. The lamellæ are formed without regard to functional stresses and Haversian systems are irregularly disposed.

**Course of the Disease** Osteitis deformans is a disease of insidious onset and slow progress and often first comes to notice on account of curvature or fracture of one of the affected bones or of the increase in the size of the head leads to its recognition. Occasionally the excessive sclerosis of small areas of the bones may culminate in sequestrum formation, and with the access of mild infection an ulcer may result. Sarcomatous change is not uncommon, and is said to occur in 5% of cases.

**Pathogenesis** Little definite is known about the cause of osteitis deformans. It appears certain that the disease is not hereditary, that it is not related to syphilis or to bacterial infection. The generalized distribution of the pathological changes strongly suggests that the fundamental factor is disturbance of the endocrine control of bone metabolism. The enzyme phosphatase is constantly present in excess, but this is not a characteristic feature, for it is present in any form of generalized skeletal decalcification.



The pathological process of *osteitis deformans* has been compared to that of *osteitis fibrosa*, and it will be noted that there is the same sequence of events, primary vascularization and decalcification, followed later by new formation of bone, but in *osteitis deformans* the ultimate new bone is much more abundant and more diffusely distributed.

### CYSTS IN BONE

The following varieties of cyst may arise in bones (1) solitary or simple cysts, (2) cysts in bone tumours, (3) cysts associated with *osteitis fibrosa*, (4) hydatid cysts.

Solitary or simple bone cysts arise most often in childhood or adolescence. They are situated generally in the humerus, and they rarely affect other bones. The cyst usually arises in the region of the proximal metaphysis of the humerus, but as the bone elongates it gradually assumes a more distal position and ultimately may be situated several centimetres from the metaphysis.

The cyst may attain considerable size and the bone at the affected site may be reduced to a thin shell. It is then very liable to fracture. In some cases fracture appears to arrest the growth of the cyst and may allow of repair.

The cyst generally contains clear watery or slightly blood stained fluid. It possesses no lining membrane and the wall is composed of fibrous tissue or bone. Often the cyst wall contains multinucleated giant cells of osteoclast type and the microscopic appearance may resemble that of *osteitis fibrosa*. Indeed, it seems probable that the two conditions are closely allied, and that simple cysts arise from a very circumscribed area of *osteitis fibrosa* in which degeneration and liquefaction predominate.

Cysts in bone tumours arise most often in connexion with giant cell tumours, and often the greater part of the tumour becomes cystic (see Fig 72). Generally such cysts contain blood stained fluid or jelly like material and are smooth walled. They possess no distinct lining membrane and the wall is composed of tumour tissue. Cysts arise also in *chondromata*, as a result of necrotic degeneration, and cysts may arise from degenerative changes in a sarcoma, myxoma and myeloma. Multiple cysts, especially in the marrow of the metacarpal bones and the phalanges, is an occasional feature of *sarcoidosis*. The condition has been styled "*osteitis multiplex cystica*."

Hydatid cysts of bones, and cysts associated with *osteitis fibrosa* are described on pp 51 and 150 respectively.

### XANTHOMATOSIS OF BONES (*Skeletal Lipoid Granulomatosis*)

Cases of this remarkable disease were described, under various titles, by Thomas Smith in 1865, and later by Hand, by Schuller and by Christian, but its true nature was not understood until 1925.

It is characterized by the development of multiple tumours in certain bones, and in most cases, by *exophthalmos*, *diabetes insipidus*, and inflammation of the mouth and gums. Occasionally the disease has

been associated with dwarfism, jaundice, and dystrophy of the adiposogenital type.

The disease occurs most often in young children, but is encountered occasionally in adults. There is no evidence of a racial or familial incidence. In approximately one third of the cases, the disease progresses and soon proves fatal. In the remainder, spontaneous remissions occur, and if early treatment is instituted, especially by adequate X ray therapy, the progress may be arrested and complete healing ultimately achieved.

**The Bone Lesions** The most characteristic feature of the disease



FIG 63 Xanthomatosis of bones. The radiogram shows the characteristic defects in the bones of the skull.

is the development of multiple tumours of xanthomatous type. In the great majority of cases the tumours are limited to bones formed in membrane, especially the cranial bones and the mandible. Less often the scapula and pelvis are involved, rarely the long bones of the extremities.

The tumours are multiple, rounded and well circumscribed. In some cases they are palpable under the scalp, or they may cause exophthalmos or other pressure effects. They are readily recognizable on X ray examination, which demonstrates large, irregularly rounded defects in the bones, not unlike the lesions characteristic of osteitis fibrosa.

The microscopic appearance of the tumours is closely similar to that of xanthoma in the skin and subcutaneous tissues. The tumours are composed mainly of large endothelial cells, with small, dark, rounded nuclei and a delicate reticular cytoplasm. These "foamy" cells owe

their appearance to the presence of numerous minute globules of cholesterol esters lying within the cytoplasmic network.

When healing takes place, either by spontaneous remission or as a result of X ray therapy, the lipid laden cells are replaced by young fibrous tissue, and later by new bone, so that eventually it may be difficult on X ray examination to recognize where the tumours had been situated.

**Other Lesions** In a small proportion of cases the bone lesions form the only recognizable feature of the disease. More commonly, one or more of the following disorders coexist.

*Exophthalmos* is present in more than half the cases. It may be an early feature, and is probably due to forward displacement of the eyeball by a xanthomatous tumour arising in the wall of the orbit.

*Diabetes insipidus* is almost equally common. In a few cases it appears to be due to pressure by a xanthomatous tumour in the region of the sella turcica, but more often there is no evidence of this, and the cause and significance of the polyuria remain in doubt.

*Gingivitis* and *stomatitis* occur less often, usually in association with xanthomatous tumours of the mandible. Their clinical importance arises from the fact that tenderness along the gums, with loosening of the teeth, may afford the earliest evidence of the disease.

*The pathogenesis* is not clearly understood. In view of the frequent association with diabetes insipidus, a primary affection of the hypophysis or midbrain has been suggested. On the other hand, the nature of the cholesterol laden deposits suggests that a disturbance of the lipid metabolism is at fault. The blood cholesterol content in most of the recorded cases, however, has been within the limits of normal, and it must be admitted that at present there is no direct evidence of a metabolic disorder.

## PRIMARY TUMOURS IN BONE

### SIMPLE TUMOURS

The classification of simple tumours arising from the skeleton is complicated, and many lesions are often designated as tumours that have really no claim to this title. Confusion has arisen from the fact that such terms as osteoma and chondroma have in the past been applied loosely to any bony or cartilaginous swelling irrespective of its exact mode or site of origin. Thus "osteoma" is often used synonymously with "exostosis" for any bony mass projecting from the skeleton, and it has even been applied to the new bone formed in so called myositis ossificans and various other diseases. Similarly "chondroma" has been applied to the cartilaginous projections of chronic arthritis or of diaphyseal aclasis. Increasing knowledge of the pathological processes of many such lesions has led to their exclusion from the category of neoplasms, and others at present retained will no doubt follow in the course of time, so that eventually the group of simple bone tumours may shrink still further.

#### Osteoma

**Compact Osteoma (Ivory Exostosis)** This rare "tumour" occurs most often in relation to the skull bones, especially the frontal or

parietal bones. It may project on the outer aspect of the skull where it forms a smooth rounded or conical projection under the scalp, or it may grow into the frontal sinus or project from the frontal bone into the orbit. Rarely it grows from the inner table of the skull and indents the brain and occasionally it lies in relation to the external acoustic meatus or inside the maxillary air sinus.

The tumour grows very slowly but in the course of many years it may attain large proportions. At first it is round or hemispherical, but, with increase in size, it becomes irregular and somewhat lobulated. In consistence it is extremely hard throughout and it may be polished like ivory. Its principal effects are from pressure upon neighbouring structures. When situated close to the skin it may lead to ulceration, in the orbit, it may displace and destroy the eyeball and later protrude

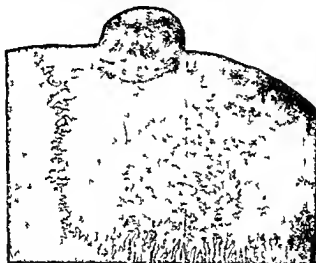


FIG. 69. Compact osteoma of the parietal bone. The tumour is smooth rounded and as hard as ivory.  
(Department of Forensic Medicine, University of Edinburgh.)

on the surface. In the acoustic meatus it predisposes to infection and may cause deafness. It is of interest to note that a large osteoma may separate spontaneously, presumably from interference with its nutrition. Bland Sutton has recorded a case of an orbital osteoma which after destroying the eyeball finally shed itself spontaneously.

Similar in appearance to an osteoma, but actually an example of heterotopic ossification is the bulky symmetrical intracranial osteophyte affecting the dural aspect of each half of the frontal bone. It occurs most frequently in aged debilitated or bedridden subjects and is probably due to deposition of bone in the fluid-filled space resulting from recession of the brain and dura mater from the frontal bones as a result of prolonged recumbency. The bony masses produce no pathological effects.

The *puerperal intracranial osteophytes* ( 'hoarfrost osteophyte' ) which coat the inner table of the skull with a veneer of new bone are also examples of ectopic bone formation following upon deranged calcium

metabolism. They are encountered as a rare complication of eclampsia or puerperal sepsis.

**Cancellous Osteoma.** It is doubtful whether this should be regarded as a true neoplasm or as a manifestation of some disturbance of bone growth closely allied to diaphysal achesis (see p. 129). For this reason it is sometimes known as a *biotrophic osteoma*. It consists of a spur of cancellous bone, projecting from the neighbourhood of a metaphysis. The most common situation is in the neighbourhood of the knee, but almost any bone may be affected. From the time of its appearance in adolescence up to the age of twenty or twenty-five years, the osteoma is capped by a layer of hyaline cartilage, which is probably a displaced portion of the epiphyseal cartilage. As it grows it becomes pedunculated and lies obliquely, directed away from the neighbouring epiphysis. In some cases the tumour is more sessile, irregular in shape, and with a massive cartilaginous cap. Such a tumour is sometimes called an *osteochondroma*.

At first the tumour is situated close to one margin of the epiphyseal cartilage, but as the diaphysis increases in length it comes to lie nearer to the mid-point of the shaft. At about the time when the epiphyses of the parent bone fuse, the cartilaginous cap of the osteoma becomes ossified and the tumour then ceases to grow.

A cancellous osteoma may cause pain from pressure on a nerve, but often it is symptomless and is recognized only on chance examination. An adventitious bursa may form over it and may become inflamed. Rarely the osteoma may be fractured from minor degrees of violence.

Other bony swellings, sometimes termed osteoma, are described in other chapters (see "Traumatic Osteoma," p. 214).

### Chondroma

As has been mentioned above, the term chondroma is applied loosely to many cartilage-containing swellings attached to the skeleton, regardless of their mode of origin. It has been applied, for example, to the cartilaginous masses that occur in dyschondroplasia or in rickets, and to those arising from the synovial membrane and joint margins in chronic arthritis. It is doubtful if such masses, associated as they are with recognizable dystrophies or diseases, should be regarded as true neoplasms.

Chondromata arise usually from the metacarpal bones and the phalanges of the hands, and are then usually multiple. Often such multiple chondromata occur in the subjects of diaphysal achesis, a

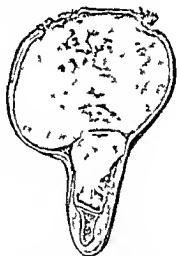


FIG. 70. Multiple chondromata of the index finger. The proximal phalanx is replaced by a rounded tumour and the second phalanx contains a small one of similar appearance. Note the areas of mucoid degeneration.

(By courtesy of Mr J. W. Struthers.)

remarkable example of tumours arising on the basis of a generalized growth disturbance. Less commonly a chondroma arises from the scapula, ribs, pelvic bones, and long bones of the extremities. The tumours appear usually in childhood or adolescence and they grow slowly over a period of years. When general growth of the skeleton ends the tumours may also become stationary.

Chondromata often grow near an epiphyseal cartilage. At first they sometimes lie in the substance of the bone (enchondroma) and they may remain there, but as they increase in size they usually project under the periosteum (exochondroma). One or more of the tumours may



FIG 71 Multiple chondromata. A radiogram from a woman aged thirty-seven years the subject of diaphyseal aclasis. All the metacarpals and phalanges are affected by chondromata, some situated inside and expanding the bones, others projecting at the surface. Three of the larger tumours had undergone mucoid degeneration.

(Department of Surgery, University of Edinburgh.)

attain considerable size and may lead to much deformity and disability.

The growths are lobulated, smooth on the surface, and covered by a layer of fibrous tissue derived from the periosteum. Often a thin shell of bone is present, and there may be bony trabeculae between the lobules.

The microscopic appearance is like that of normal hyaline cartilage, but the cells are arranged irregularly and vary in size and shape. Necrosis or mucoid degeneration often takes place, and leads to one form of bone cyst. Calcification is common, and sometimes ossification occurs. Sarcomatous change is rare.

### Giant-cell Tumour

(Tumeur à myélopaxes, osteoclastoma, myeloid sarcoma, myeloma.)

This is one of the most striking of bone tumours, and its clinical and pathological features are uniform and characteristic. Unfortunately the terminology is complicated and misleading. Since the tumour does not infiltrate except to a very limited extent, and only gives rise to metastases in exceptional cases, it is fitting that the old name *myeloid sarcoma* should be discarded. The term *myeloma* should also be abandoned, for it is almost certain that the tumour does not arise from bone marrow, and moreover "myeloma" leads to confusion with "multiple myelomata," an entirely distinct form of neoplasm.

The origin of the giant cell tumour of bone has been a subject of controversy since the time of Nélaton who was the first to describe it adequately. Nélaton

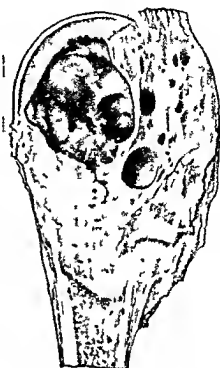


FIG. 72. Giant cell tumour of bone arising at the proximal metaphysis of the humerus. The tumour has expanded the bone and forms an ovoid mass partly solid and partly cystic.

(By courtesy of Mr J. W. Struthers.)



FIG. 73. Radiogram of a giant-cell tumour at the distal end of the radius. The tumour is situated close to the metaphysis and has expanded the bone. The lobular character is clearly seen.

believed that the tumour originated in bone marrow and he regarded the giant cells as modified myeloblasts or megakaryocytes. At the present time, however, it is generally thought that the giant cells are derived from osteoclasts, the foreign body giant cells normally engaged in bone resorption.

The giant-cell tumour of bone occurs in either sex and at any age, but generally it is found between the ages of fifteen and thirty years. In a large proportion of cases the tumour arises in a bone of the lower extremity. Like bone sarcoma it is situated most frequently close to the knee, especially at the distal end of the femur. Any long bone, however, may be affected and giant-cell tumours have been found in the bones

of the upper limb in the scapula and the pelvic girdle. It is found in such situations as the distal end of the radius, tibia or fibula, relatively rare sites of sarcoma. It is not uncommon in the jaws.

The tumour originates either in the metaphysis or in the epiphysis, where it forms a localized well demarcated growth, often more or less globular in shape. It may grow eccentrically, and reach the surface of the bone on one aspect only, or it may enlarge concentrically. Unlike a sarcoma, it is sometimes not restrained by the epiphysal cartilage, and may spread as far as the articular cartilage. Penetration of the joint is exceptional.

The tumour is composed of soft, cellular, very friable and often jelly-like tissue, which is usually very vascular, and from hæmorrhage may be of a dark reddish purple or maroon colour, and aptly likened to red currant jelly. The tumour is traversed by delicate fibrous or bony



FIG. 74. Giant-cell tumour of bone.  $\times 300$ . Note the giant cells of characteristic appearance and the stroma of small spindle-shaped cells.

trabeculae, which in radiograms give a characteristic honeycomb or mosaic appearance. The central portions frequently undergo cystic degeneration, and occasionally one large cyst replaces the greater part or even the whole of the tumour.

The soft tissues are invaded only in exceptional cases, and the tumour usually remains surrounded by a thin shell of bone. Even when a tumour has attained large size there still remains a thin covering of new bone beneath the periosteum—a complementary process of bone resorption and replacement which is loosely termed "expansion."

Although the above description applies to the vast majority of these tumours, a few examples have been described, principally at the distal end of the radius, which differ in being relatively avascular—so called "white" giant-cell tumours.

*Microscopically*, the tumour consists principally of a spindle cell stroma in which are scattered giant cells of characteristic appearance. The giant cells vary in number in different tumours and in different



parts of the same tumour, but their appearance is remarkably uniform, and is identical with that of foreign body giant cells. They contain numerous nuclei and an abundant homogeneous cytoplasm. The nuclei usually number from 10 to 20, but as many as 100 may be present. They lie principally in the central part of the cell, and are sometimes arranged like a rosette. Each nucleus is distinct from its fellows and of uniform appearance—small, rounded or oval, and intensely basophilic.

The stroma may be fibrous or cellular, the latter being to some extent an indication of rapid growth. The cells are small and principally spindle-shaped. Mitotic figures are rare. Occasionally scattered through the stroma are collections of large clear "foamy" cells containing an abundance of doubly refractile lipid material—a form of xanthoma. The blood vessels are numerous, large and thin walled.

**Progress and Effects of Giant-cell Tumours.** Giant cell tumours usually progress slowly, and for a considerable time may cause little disability. Often the tumour remains unrecognized until a fracture occurs a fairly frequent complication. In other cases weakening or even collapse of an adjacent joint may occur from penetration of the epiphysis. Rarely the growth of the tumour appears to be arrested spontaneously, and sometimes from central liquefaction the whole mass becomes converted into a single large bone cyst, in the fibrous walls of which only small traces of the original tumour are still to be found.

*Malignant change* may occur, though not commonly. The frequency of this complication is a matter of great practical importance to the surgeon, who is faced with the necessity for deciding between amputation and local attack upon the tumour. There is no doubt that in rare cases the tumour is actually malignant, for a few authentic cases have been reported in which pulmonary metastases developed and it is equally certain that occasionally the tumour undergoes sarcomatous transformation after an early simple course, and gives rise to round cell or spindle-cell metastases. In the great majority of cases however, the tumour is essentially non malignant, and there is thus ample pathological evidence to warrant the conservative measures in vogue at present, especially as in most instances the 'tumour' cells are sensitive to irradiation.

## MALIGNANT TUMOURS OF BONE

Since the days when all soft tumours of bone were thought to be cancers there have been many changes in their nomenclature and classification. The first important advance was the segregation of *secondary tumours* and later the recognition of the various types of *primary tumours*. In recent years our knowledge of this latter group has been greatly increased and clarified by the work of those connected with the Registry of Bone Sarcoma in the United States of America and for the first time accurate information has become available upon many aspects, clinical and pathological of a large series of cases. According to the Registry classification, the malignant primary tumours of bone may be divided into the following principal varieties—

- (1) True bone sarcoma (osteosarcoma osteogenic sarcoma)

including periosteal sarcoma, central sarcoma, sclerosing sarcoma and telangiectatic sarcoma

- (2) Tumours of bone marrow—multiple myeloma
- (3) A tumour of doubtful nature—endothelial sarcoma or Ewing's tumour
- (4) A group of uncommon and unclassified tumours

#### Bone Sarcoma (Osteo-sarcoma, Osteogenic sarcoma)

This is the commonest of the primary malignant tumours of bone, and it is said to account for 30% of all sarcomata. It affects males

somewhat more often than females, and it occurs with overwhelming frequency in the second decade, the period of most active skeletal growth. In patients over fifty years of age it is very uncommon, except as a complication of some dystrophy such as osteitis deformans. In its pathological aspects the disease is one of great complexity, but its clinical features and end results are only too uniform, for, with very few exceptions, its malignancy is extreme, and even after early radical treatment a fatal issue is not long delayed.

Bone sarcoma usually arises in or near that part of the bone in which proliferative changes normally progress most actively, namely, the metaphysis. Not infrequently, moreover, it supervenes upon other bone diseases, such as osteitis fibrosa or osteitis deformans (the last named alone accounting for about 5%) and it is significant that all these diseases are characterized by profound disturbance of the processes of bone growth and repair. In some cases trauma appears to determine the onset of the tumour.



FIG. 75. Sarcoma of the femur in a young person. The tumour appears to have originated near the distal metaphysis and has extended far both along the marrow cavity and under the periosteum. Note that it has not penetrated the epiphyseal cartilage nor involved the joint.

(Department of Surgery, University of Edinburgh.)

Bone sarcoma is generally regarded as arising from bone-forming cells (osteoblasts), but it is not necessarily composed of bone, for bone formation is only a potential property of these cells, and when malignant they revert more closely towards the embryonic state and lose their bone-forming habit. In some tumours this reversion is almost complete and the cells produce only a delicate mesenchymal stroma, and the tumour remains soft and fleshy; or they may differentiate in greater or less degree and produce mucoid material, cartilage, or bone.

To emphasize this supposed origin of the tumour from bone-forming cells or their non-bone-forming derivatives, Ewing has suggested the title *osteogenic sarcoma*, and this name has obtained wide acceptance, particularly in America. The term is, however, unfortunate in this sense—that it is often interpreted as “bone producing,” the antithesis of its intended meaning.

**Types of Bone Sarcoma.** Classifications of bone sarcoma are clumsy and confused, and very perplexing to the student. Fortunately the general trend at present is towards simplification, and this has been assisted by the work of the American Registry. The following principal types may be recognized:—

(1) *Periosteal Sarcoma.* This is the commonest type. The greater part of the tumour lies deep to the periosteum, and raises it off the bone cortex, but the tumour also infiltrates the substance of the bone and may extend along the medullary cavity. In some cases the tumour appears to arise from the periosteum; in others it is probably derived from the connective tissues continuous with the periosteum that penetrate the bone and line the bone spaces.

(2) *Medullary or Central Sarcoma (Endosteal Sarcoma).* Tumours situated within the bone, and not extending to the surface,

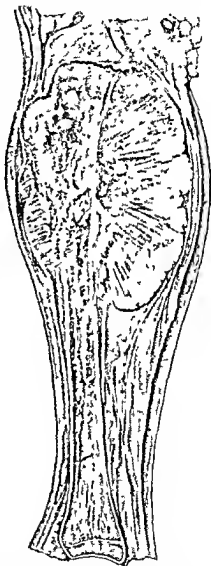


FIG. 76 A bone sarcoma arising at the proximal metaphysis of the tibia. The tumour has infiltrated the marrow cavity and has elevated the periosteum. Proximally it is limited by the epiphyseal cartilage. Note the radiate spicules of new bone formed in the tumour. (Museum of Royal College of Surgeons of Edinburgh)

figure largely in older surgical descriptions, but modern experience shows that sarcoma of this class is rare

(3) *Sclerosing or Ossifying Sarcoma* This type is characterized by the formation of a large amount of new bone in the tumour. In some cases the tumour is extensively ossified, even to the hardness of ivory. The new bone formation is generally looked upon as evidence of some kind of defensive reaction on the part of the tissues, but there is little proof that a sclerosing sarcoma is any less malignant than other varieties

(4) *Telangiectatic Sarcoma (Malignant Bone Aneurysm)* In some bone sarcomata the vascularity is so great that the greater part of the tumour is occupied by blood vessels, which are large and extremely



FIG 7. Bone sarcoma.  $\times 275$  A spindle-cell sarcoma of the tibia. The tumour is highly cellular. It is composed of elongated spindle-shaped cells some of which have been cut transversely and consequently appear to be rounded.

thin walled. Sometimes, indeed, the blood vessels have no complete endothelial lining, but are mere spaces surrounded by the malignant tumour cells. The vascularity may be such that the tumour pulsates. Since the tumour cells have ready access to the blood stream the risk of early metastases is very great, and the outlook is correspondingly grave. This type of tumour is especially apt to affect young subjects.

**Morbid Anatomy** The ends of the long bones of the extremities are affected with greatest frequency, but such irregular bones as the jaws, the scapula and the bones of the pelvic girdle are by no means exempt. It is estimated that the bones of the lower limb are involved in about 70% of cases, the distal end of the femur and the proximal end of the tibia being most frequently affected. In the upper limb the proximal end of the humerus is the site of election. The regions of the wrist and ankle joints are very rarely involved (compare giant

cell tumour), and sarcoma of the smaller bones of the hands and feet is exceptional

In a typical example of a sarcoma near the end of a long bone the growth extends widely along the paths of least resistance, permeating the interstices of the bone and eroding its lamellæ. It extends along the marrow cavity, permeates the cortex and erupts on the surface. The periosteum for a time resists invasion and becomes raised from the surface of the bone, and deep to it the tumour spreads widely so that eventually it may form a fusiform mass ensheathing the bone extensively.

Often the tumour consists of two main portions, an elongated, ill-defined mass permeating the marrow cavity and an ensheathing growth

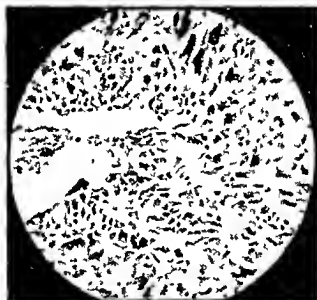


FIG. 78. Bone sarcoma. A spindle-cell sarcoma of the femur. Note the large blood space on the left. It is thin walled and in places it lacks even an endothelial lining and is in direct contact with the malignant cells.

(Department of Surgery, University of Edinburgh.)

under the elevated periosteum, the two portions being separated in much of their extent by the more resistant cortical bone. If with further progress the tumour perforates the periosteum, it extends widely within the soft tissues, causing great swelling and œdema with dilatation of the superficial veins. The skin becomes tense and glossy, but for a long time it resists actual invasion and ulceration. The epiphysis is rarely invaded, and since the periosteum is attached to the circumference of the epiphysal cartilage the joint is not affected until late.

The appearance of the tumour varies greatly. Most often it is soft, red, fleshy and very vascular, with areas of hæmorrhage and necrosis. In other cases the appearance is modified by the presence of cartilage or of bone. Cartilage renders the tumour more firm, with bluish translucent areas (chondrosarcoma, see p. 169). Bone of new formation is usually present in greater or less amount. When new bone

predominates the marrow cavity may be obliterated and the whole end of the diaphysis be increased in circumference by a fusiform mass of bone, which sometimes assumes ivory like hardness. This is called the sclerosing type.

**Microscopic Appearances** The microscopic features of bone sarcoma are complex. The tumour cells show great diversity and the picture is complicated by such secondary processes as bone resorption or new bone formation.

The predominating type of cell is small and spindle-shaped, but large, polyhedral and even round cells may occur. The cells are hyperchromatic and with frequent mitoses often of irregular type. Giant cells of the 'malignant giant-cell' type are often present. Cells of this type have a characteristic appearance, very different from the cells of the so-called *giant-cell tumours*, they are irregular in shape and size and contain few nuclei which are oval or indented, joined together, and deeply hyperchromatic.

One of the most conspicuous features is the structure of the blood vessels. They are large and thin walled and in close relation to the tumour. In places even an endothelial lining is lacking and the blood flows in large clefts lined by tumour cells, consequently there is a great liability to liberation of malignant emboli.

**Ossification in Bone Sarcoma** The production of new bone is a characteristic feature of nearly all cases of bone sarcoma. The new bone is laid down principally under the periosteum. In some cases there are radiating spicules developed like stalagmites perpendicular to the

surface of the bone. Such new formations have a characteristic 'sun ray' appearance in radiograms. The disposition of the spicules appears to depend upon the arrangement of smaller vessels extending perpendicularly from the elevated periosteum into the cortex. Less often the new bone takes the form of a small wedge shaped ossification which occurs where the periosteum is elevated beyond the advancing edge of the tumour.

**Metastases in Bone Sarcoma** Metastatic deposits are of extremely common occurrence, hence the almost uniformly bad prognosis. Owing to the intimate relationship of the vessels to the tumour, blood borne emboli are common and the lung is the most frequent site of their arrest. Less commonly, or in the later stages, other viscera and other bones may be affected. It would appear that the metastases occur



FIG. 79. Bone sarcoma arising at the distal metaphysis of the femur. Macerated specimen which shows much new bone laid down as spicules perpendicular to the surface of the femur.

(Museum of Royal College of Surgeons of Edinburgh.)

early, but may grow slowly. They are probably often present at the time of operation, but only after a period of months do they become obvious. Microscopically, the metastases tend to reproduce the varied structure of the original growth, and they may contain fibrous matrix,

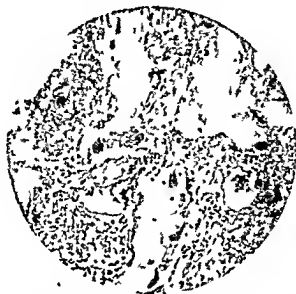


FIG. 50. Bone sarcoma of telangiectatic variety. The bone trabeculae have undergone resorption, and the intervening spaces are occupied by tumour cells. Note the large number of osteoclast giant cells which lie in a position to the bone trabeculae.

and cartilage but it is remarkable that metastases in soft tissues such as the lungs rarely produce bone.

### Chondrosarcoma

(Chondrifying sarcoma, sarcomatous chondroma.)

Strictly speaking, the term chondrosarcoma should be restricted to a simple chondroma which has undergone malignant change, but in practice it is understood to include any sarcomatous tumour containing cartilage in excess. The majority occur in relation to the ends of long bones, forming bulky lobulated masses which on naked eye inspection resemble simple chondromata, but microscopically show also sarcomatous elements in varying proportion. This type of tumour is now generally regarded as a bone sarcoma with a predominance of cartilage matrix rather than as a specific type.

In their malignancy and course these tumours vary greatly. They are particularly insensitive to irradiation. A peculiar feature is a tendency to extend along the lumen of blood vessels and such a growth has been known even to reach the heart. Multiple secondary growths are frequent, but sometimes a solitary metastasis appears and attains considerable size before the disease becomes generalized.



FIG 81 Chondrosarcoma of the femur. The shaft of the femur is permeated by solid tumour tissue. The outer parts of the tumour are composed of lobules of jellylike material separated by fibrous trabeculae.

(By courtesy of M. J. W. Stenhouse)

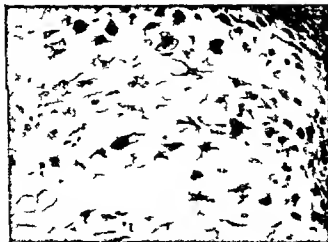


FIG 82 Chondrosarcoma undergoing mucoid change. Many of the cells are distended to a gnet ring shape by large globules of mucoid material and the intercellular substance is infiltrated by a similar material.

(Department of Surgery, University of Edinburgh)



## Multiple Myeloma (Plasmacytoma)

This rare disease is characterized by the development of multiple tumours in many parts of the skeleton. It is a disease of adult life, occurring usually between the ages of forty and sixty, and commonly in men. Any part of the skeleton may be involved, but the tumours are usually most evident in the sternum, the ribs, the vertebrae, the skull and the femora.

The tumours are usually small, but occasionally they may grow to the size of walnuts and a few attain even greater dimensions. They invade any part of the bones, but mainly the marrow cavity, and form rounded or oval well circumscribed masses of grey or greyish red colour and of soft consistency. Adjacent bone is invaded by the tumour and is decalcified, without any new bone formation, so that when the bone is extensively affected the condition may bear a superficial resemblance to osteitis fibrosa or to metastatic carcinomatosis. The bone may be so thinned that fracture results, and in the later stages the tumours invade the surrounding soft parts. The growth of a tumour in the vertebral column commonly leads to severe pain and eventually may cause compression paraplegia. In the later stages of the disease there is a considerable degree of anaemia, doubtless resulting from destruction of the red marrow.

A well known feature of the disease, is the excretion of proteose in the urine (Bence Jones). The proteose, which may appear in enormous amount, gives the ordinary reactions for this class of substance, and is recognized by its behaviour when heated. At a temperature of about  $55^{\circ}\text{C}$  the urine becomes opaque, and a sticky coagulum forms on the surface. On heating further, to the neighbourhood of  $85^{\circ}\text{C}$  it disappears, but forms again when the urine cools. Similar proteosuria occurs also though in small amount in certain cases of leukaemia, in secondary tumours of the skeleton, and occasionally in nephritis.

The serum globulin is increased from the normal of 1.6-2.5% to as much as 7%. Occasionally, owing to rapid decalcification,

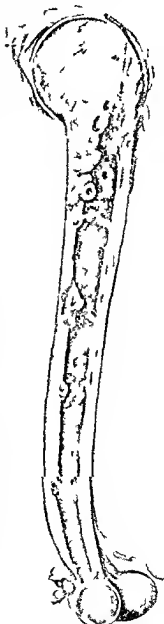


FIG. 83. Multiple myeloma. Numerous small rounded tumours occupy the head and shaft of the humerus.

(Department of Pathology, University of Edinburgh.)

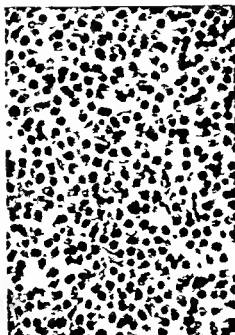


FIG. 24 Plasmacystoma (multiple myeloma). The tumour contains many plasma-cytes, large oval cells of which the nucleus lies eccentric and has a coarse meshwork of chromatin.  
(Department of Pathology University of Glasgow.)



FIG. 25 Multiple myeloma of scapula and clavicle. Radiograph of specimen.  
(Department of Pathology University of Glasgow.)

the serum calcium is raised. Parathyroid osteitis may then be suspected but can be excluded by the observation that, in myelomatosis the plasma phosphorus is not decreased and the phosphatase is normal.

Microscopically, the growths are composed of diffusely arranged round cells with little or no intercellular substance. Usually the cells are of the plasma cell type, with deeply basophil cytoplasm and a small eccentric nucleus but sometimes cells of lymphocyte type, or cells resembling the primitive white cells or myelocytes, may preponderate. In exceptional cases erythroblasts have been described. The condition is generally regarded as a disease of the blood forming tissues rather than of bone, and the cells are believed to originate in the bone marrow. They can nearly always be demonstrated by marrow puncture. It is true that plasma cells do not occur in the marrow under normal circumstances, but they are presumed to be related to the other more definitely hematopoietic cells. In this connexion it is interesting to note that the spleen is usually enlarged, as in leukaemia and lymphadenoma, and that visceral metastases occur in the liver and the spleen and occasionally in the lymph glands, but not in the lungs.

**Solitary Plasmacytoma** In rare instances, especially in middle age, a plasmacytoma may be single and without other bony changes. It is sometimes the first evidence of a more generalized affection of the skeleton. The tumour frequently comes to notice as a result of a pathological fracture of one of the limb bones, rarely a vertebra. The tumour occurs centrally in any part of the shaft of the bone which shows rarefying osteitis. —Rare sites are the nasal sinuses and the trachea. The tumour is amenable to surgical or radiotherapeutic treatment, especially the latter.

### Endothelial Sarcoma (Ewing's Tumour)

This tumour has only been recognized as a distinct type in recent years, and it seems possible that most bone tumours hitherto called small round cell sarcoma belong to this type. Since Ewing first described it a number of cases have been recorded, chiefly in America, and according to the figures of the Registry of Bone Sarcoma it is not uncommon, its occurrence is variously estimated at from 7% to 10% of all primary malignant tumours of bone. It is commonest in young persons, particularly between the ages of five and fifteen, and it is three times commoner in males than in females. A history of recent injury is often obtained. The long bones, the tibia, humerus and femur, are those most frequently affected, but the tumour may occur in the short bones of the extremities, particularly in the calcaneus.

The tumour differs from other varieties of sarcoma in that it arises usually from the mid part of the diaphysis of the bone. It arises in the bone marrow, and spreads in all directions from its point of origin, penetrating the bony lamellae to reach the surface of the bone. The periosteum at first resists invasion, and layer after layer of new bone is formed and subsequently eroded.

The appearance of the tumour is remarkable, for it is soft, greyish-white in colour and somewhat brain like, often with semi-housefied

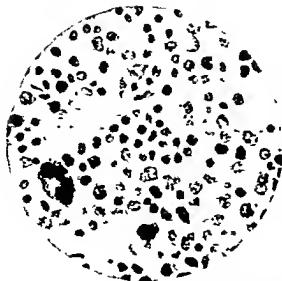


FIG. 86. Multiple myeloma.  $\times 450$ . The greater number of the tumour cells are myeloblasts—primitive white blood cells—in addition to a few giant cells.

areas of degeneration which may resemble pus. When such material is seen lying between partly eroded bone lamellæ the appearance suggests osteomyelitis, for which it is often mistaken.

The first symptom is usually pain, and this is often intermittent, recurring in attacks of increasing severity over a period of weeks or months. The swelling appears later and may vary in size, retrogression being accompanied by temporary relief of symptoms. Pathological fracture may occur, but is not very com-

mon. There is often a slight leucocytosis and secondary anemia. The tumour responds well to radiation, and by suitable treatment its growth and spread may be controlled for a considerable period. Finally, however, metastases appear in other bones and in lymph glands and viscera, and the disease eventually proves fatal.

The microscopic appearance is noteworthy for its simplicity and uniformity, contrasting greatly with the pleomorphism of other sarcomata of bone. The tumour is composed entirely of small rounded or polyhedral cells, arranged in coherent sheets with little or no intercellular substance. Sometimes the masses of cells are embedded in a delicate connective



FIG. 87. Ewing's tumour. The tumour is composed of polyhedral cells with little intercellular material.

tissue framework, but often this is lacking. From degeneration of the portions furthest from their source of nourishment a perivascular grouping of the surviving cells often results. Mitotic figures are numerous.

The origin of Ewing's tumour is not clear. Most authorities regard it as derived from the perivascular endothelial cells of the marrow. Recent work suggests that many supposed cases of Ewing's tumour have actually been examples of metastatic growths, secondary to bronchial carcinoma or to neuroblastoma of the adrenal gland.

### Endothelioma of Bone

Until recent years "endothelioma" was the graveyard of unclassifiable tumours, but since the adoption of stricter histological standards for endothelial cells these tumours are now acknowledged to be rare. Endotheliomata of bone described in recent years have resembled bone sarcoma, both in the clinical course and in their pathological aspects, the diagnosis being made only by microscopic sections, in which cells of endothelial type are seen apparently arising from the internal coat of vessels and forming nidi or tubules, which in some cases contain blood.

### Parosteal Fibrosarcoma

This tumour also appears to be rare, but it is of interest in that it is believed to account for a certain proportion of the "cures" of bone sarcoma, the malignancy being relatively low and the prognosis correspondingly good. Strictly, it is not a bone tumour, but arises on the outer aspect of the periosteum, and forms a fairly well encapsuled mass in the soft tissues, and leads to little or no erosion of the bone. Microscopically, it resembles a cellular fibroma, and is composed of elongated cells embedded in a scanty fibrous stroma. Since the tumour adheres to the periosteum it appears on clinical examination to be fixed to the bone, and it may spread to some extent around the bone as a sheath. Invasion of the surrounding parts is a late occurrence, as are metastases, and the outcome of radical excision is therefore promising.

## SECONDARY TUMOURS IN BONE

Bone is a common site for secondary tumours derived from various types of primary growths. Such secondary tumours may arise (1) by local extension of the primary growth, or (2) by dissemination of cells along the lymph or blood vessels.

(1) Involvement of a bone by the direct extension of a malignant tumour is a familiar occurrence. It is observed when a carcinoma of the tongue or the floor of the mouth invades the mandible, when a rodent ulcer or lupus carcinoma of the face destroys the bones of the skull (Fig. 88), or when a carcinoma that has arisen in a chronic leg ulcer invades the tibia.

In bones thus involved decalcification and destruction are the most outstanding changes and are aggravated by superimposed infection. As in other conditions in which hyperæmia affects bone, a gradual process of decalcification occurs and the bone becomes softened and replaced by the extending tumour, so that in a macerated specimen it has a worm eaten or sand papered appearance. Usually no new

bone is formed at the extending margin of the tumour or within the tumour itself, unless the invading tumour is one of great vascularity, when bone resorption and new bone formation may occur simultaneously. In such instances the new bone is represented by light spicules of feathery appearance that project into the tumour from the surface of the bone on which it impinges.

(2) Involvement of bone by malignant cells disseminated from a distant growth occurs most commonly in cancer of the breast, prostate and bronchus, less often in cancer of the kidney, and in the late stages



FIG. 88 Destruction of the facial bones as a result of invasion by lupus-carcinoma.

(Museum of Royal College of Surgeons of Edinburgh.)

of many other types of cancer. Malignant tumours of the thyroid gland commonly metastasize to bone, but this growth is somewhat of a rarity.

Certain bones are especially liable to be the seat of metastatic growths. The ribs, vertebrae, sternum, skull, pelvic bones, femur, and humerus are commonly affected, and less often the mandible, scapula and clavicle. The distal bones of the extremities are rarely involved.

Evidence is overwhelming in favour of the view that most metastatic bone tumours result from blood borne emboli of malignant cells. Such cells derived from any source other than a primary tumour of the lung must be presumed to have passed through the pulmonary circulation before reaching the systemic circulation, and the possibility of this

occurrence is well recognized. The work of Schmidt is of great importance in showing how malignant emboli may behave on reaching the lungs, for it has shown that the cancer cells may grow directly from the pulmonary arterioles into the capillaries and veins without invading the vessel walls. In this way metastases may be disseminated by the systemic circulation yet leave no trace in the lungs.

It has been claimed that in some cases metastatic bone tumours result from permeation of the lymph vessels by malignant cells but the evidence for this view is somewhat slender, for lymph channels have not been demonstrated in the bone marrow, and the lymph vessels of the cortex do not extend beyond the endosteum. Moreover, bone metastases begin centrally, and often at a very considerable distance from the primary growth, and it is rarely possible to demonstrate



FIG. 50. Metastatic growths in the bones of the skull. The primary tumour was a cancer of the stomach. The metastases have led to decalcification and erosion of the bones. No new bone has been formed.  
(Museum of Royal College of Surgeons of Edinburgh.)

involvement of intermediate lymph channels. (See also chapter on Diseases of the Breast.)

The principal evidence in favour of lymph spread to bone is the special liability of certain bones to metastatic growths and the comparative immunity of other bones, but Piney has advanced a reasonable explanation for this "selectivity," which accords well with the theory of haematogenous spread. He points out that the sites mentioned above are precisely those where red bone marrow persists in adult life, and that the sinusoidal character of the circulation in the red marrow, by its almost stagnant condition favours the lodgment and proliferation of cancerous emboli. When a metastatic growth is found at sites where red bone marrow is not present normally, for example, in the shaft of the tibia or in the small bones of the hand, it has been suggested that the constitutional effects of the malignant disease, e.g., secondary anaemia, have been such as to stimulate an erythroblastic reaction in the marrow, which would afford a favourable site for the growth of cancer cells.

The blood changes are often characteristic. There is usually

hypochromatic anemia, and the red cells and leucocytes are of immature type. There is a low platelet count. The degree of anemia does not bear a definite ratio to the extent of the metastasis.

**The Changes in the Bones** The effects of metastatic tumours upon the bone are characterized principally by decalcification and destruction. When small, a metastatic tumour appears as an opaque, greyish focus in the interior of the affected bone, and causes no striking change in it, but as the tumour grows the adjacent bone becomes encroached upon and rarefaction occurs for some distance around. With the exception of metastases from carcinoma of the prostate, new bone is formed only in rare instances. A localized spherical or ovoid expansion of the bone occurs, but this enlargement is rarely very considerable. A thin shell of bone usually circumscribes the tumour and the periosteum remains intact. If the affected bone is submitted to undue strain, fracture readily occurs.

In the spinal column several vertebrae may collapse, resulting in the development of kyphosis, and/or pressure on the cord or on the spinal nerves. At the site of fracture there may be a considerable attempt at repair by new bone formation, but firm union is very rarely attained.

Other characteristic features of bone metastases vary according to the situation and nature of the primary growth.

*Cancer of the breast*, from its relative frequency, is the most common source of the metastases. The vertebrae, ribs, and sternum are most often affected, but not infrequently deposits may be found in the upper end of the femur and of the humerus. In a few instances almost all the skeleton is affected, producing the condition sometimes known as "generalized cancerous osteomalacia." Frequently osseous metastases appear months or many years after removal of the diseased breast.

*In cancer of the thyroid*

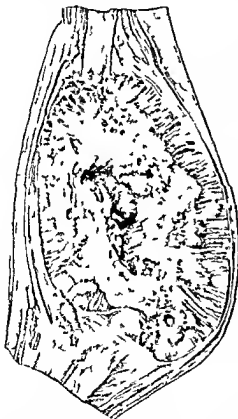


FIG. 90. Thyroid metastasis in bone. A secondary growth in the humerus from an adenocarcinoma of the thyroid. The tumour has destroyed the distal half of the bone and has elevated the periosteum. At the centre, the tumour has undergone necrosis.

(Museum of Royal College of Surgeons of Edinburgh)



gland the skeleton is one of the commonest sites for metastases. They are found most often in the vertebrae, skull, and sternum, but they may occur also in the long bones of the extremities. The primary growth which is not infrequently a malignant adenoma may be so small as to escape detection, and the thyroid gland then appears normal on clinical examination. The metastases are rarely numerous and may be single, therefore in some instances their removal may be undertaken with a favourable prospect of cure.

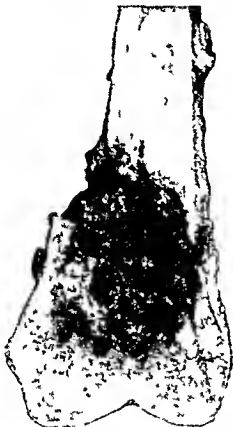


FIG 91 Secondary tumour in bone. Metastasis at the distal end of the femur from an adenocarcinoma of the kidney. The tumour is highly vascular and as a consequence the bone has undergone extensive decalcification.

(Department of Surgery University of Edinburgh.)



FIG 92 Secondary tumour in bone. Radiogram (From same specimen depicted in Fig 91)

The histological appearance of the secondary tumours is very variable. They may resemble the primary thyroid growth, they may look like normal thyroid tissue, or they may show any degree of malignancy. The secondary tumour may produce thyroid secretion, and its removal has been known to be followed by myxoedema.

*Hypernephroma of the kidney* is sometimes associated with secondary growths in bones. Usually the metastasis is single and may not be manifest until a considerable time after removal of the renal tumour and in a few instances the source of metastasis is only revealed after

thorough examination or at autopsy. Favourite sites for metastases are the upper end of the femur, the sternum, and the pelvic bones. New bone formation within the tumour is often a prominent feature.

*Carcinoma of the prostate* is often associated with skeletal metastases. It is important to recognize that no prostatic enlargement may be detected on rectal examination and in a few instances not until the prostate has been examined histologically can its malignant nature be established. Irradiation by X rays or radium of a malignant prostate has sometimes appeared to precipitate the appearance of osseous metastases. The secondary growths are generally disseminated widely,



FIG 93. Vertebral metastasis of a papillary adenocarcinoma of the kidney. Columnar epithelial cells arranged in papillary formation are invading the bone.

(Laboratory of Royal College of Physicians of Edinburgh.)

but the pelvic bones, the spine and the skull are the commonest sites.

In many instances the disseminated cancer cells excite a remarkable osteoplastic reaction which results in both increase in density and girth of the affected bone. The medullary canal is often obliterated, and a severe degree of secondary anaemia may result from destruction of the bone marrow.

It has been shown that in metastasizing carcinoma of the prostate the serum 'acid' phosphatase is increased and it has been suggested that its estimation may be helpful in diagnosis. Elevation to from 6 to 10 units is supposed to be very suggestive. The source of the increased serum phosphatase is probably the carcinomatous tissue. In the normal prostate the 'acid' phosphatase is a product of the acinar epithelium, a capacity which is apparently retained when malignant change supervenes.

It has been observed that the skeletal metastases of carcinoma of the prostate may show retrogression or may even disappear following castration. The administration of oestrogens has a similar effect in a

high proportion of cases and confers considerable relief. The observation is of special interest, for it is the only example in which a substance given by mouth has been effective in the treatment of malignant disease.

### TUBERCULOSIS OF BONES AND JOINTS

Tuberculosis of bones and joints occurs with greatest frequency in childhood, especially during the first six years of life, and only in a small proportion does it begin after the age of fifteen. Adults are not immune however, and the disease may occur even in old age. In children the process is often slow and tractable but in adults resistance is often poor, so that the progress can be checked only by radical measures.

Bone tuberculosis and joint tuberculosis are so often combined that it is appropriate to consider them together, although in some situations, *e.g.* in the vertebrae, skull, and bones of the hands and feet, the disease is confined to bone.

It has never been finally settled whether tuberculous arthritis follows disease of one of the bones or arises as a direct infection of the joint. How much it matters is seldom important. Perhaps most observers believe that in the majority the bone is affected

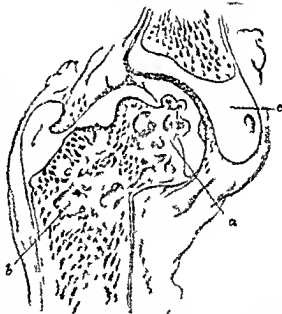


FIG. 94. Tuberculosis of the femur in a child aged two years. (a) Tuberculous granulation tissue of gelatinous appearance. (b) an area of caseation. (c) the acetabulum. The disease has originated at the metaphysis and has spread thence into the epiphysis and also down the shaft.

first, the joint later. Joint disease spreads more rapidly and causes more obvious effects than the earlier and less conspicuous bone lesion. This view is generally accepted for the majority, but it is beyond doubt that the disease sometimes affects the synovial membrane only.

The infecting organism may be of human or bovine type, and the relative frequency with which one or the other type is responsible is said to vary in different countries. In Scotland, according to Griffith, the bovine organism is present in 42.8% of cases, whereas in England the corresponding figure is 18% (see p. 36).

**The Sites Affected.** In long bones the disease usually begins in the epiphysis, rarely in the metaphysis. In the short long bones of the hand and feet, on account of their arborescing blood supply, the disease

begins in the diaphysis. Subperiosteal tuberculosis is not infrequent in adults, but is rare in children.

The relation of the synovial membrane to the articular end of the bone is an important factor in determining spread of the disease. When the capsule extends beyond the epiphyseal cartilage, as, for example, at the hip joint, the metaphysis comes into direct relationship with the synovial membrane, and consequently the joint is infected directly.

The liability to tuberculosis is not shared equally by all bones and joints. In children, the vertebrae, hips and knee are common sites, in that order of frequency. In adults the joints of the upper extremity are more liable to infection, in the order, shoulder, elbow, wrist. The knee is also a common site.

The special susceptibility in childhood, and the predilection of the disease for certain bones and joints are attributed to such factors as growth activity and exposure to injury. Growing bones appear to be more susceptible than the mature. The frequent involvement of the bones and joints of the lower extremity and of the spine is attributed to the strain to which they are exposed.

### Pathology of Bone Tuberculosis

When a bone is invaded by tubercle bacilli the effects differ in no particular from those of tuberculosis elsewhere, they are conditioned merely by the structural characteristics of osseous tissue. There is the usual evolution of tuberculous granulation tissue, so that the bone at and around the diseased area undergoes slow but progressive decalcification, hence the "osteoporosis" which forms so striking a feature in radiograms. The periosteum is but little affected,

and there is little or no new bone formation.

The disease may be "encysted" or enclosed within a fibrous capsule, or it may infiltrate widely. Extensive atrophy of the bone is a common feature, especially at the shoulder (*caries sicca*).

### Pathology of Joint Tuberculosis

The relation of joint tuberculosis to bone tuberculosis has already been discussed, and it has been stated that, by the consensus of opinion, the arthritis is usually secondary to a tuberculous focus in the adjoining



FIG. 6a. Tuberculosis of the tibia. The distal part of the diaphysis is greatly thickened by the formation of new bone, of soft, spongy character.

(Museum of Royal College of Surgeons of Edinburgh.)

bone. In a proportion of cases, especially in the knee, the joint is infected directly by blood-borne organisms.

The *synovial membrane* is usually the site of the initial infection, and it always shows greater changes than other parts of the joint. Generally, the earliest tubercles appear near the line of reflection of the synovial membrane to the bone, for this part lies in closest relation to the blood supply and to the original focus in the bone. Tubercles develop in the connective tissue of the synovial membrane, and the usual cellular response that characterizes tuberculosis elsewhere is seen.

The articular cartilage may be involved superficially by encroachment of a "pannus" of diseased synovial membrane, and become dull, pitted and eroded; or it may be undermined and cast off into the joint as a result of infection spreading in the underlying bone.

The soft tissues around the joint undergo degenerative changes that together give the appearance known as "white swelling." Ligaments and tendons become cedematous, stretched and lax, and muscles undergo atrophic changes. All the tissues are swollen and cedematous and have a pale gelatinous, glistening appearance. Not uncommonly, cold abscesses may track through the soft tissues around the joint, and ultimately form sinuses.

The *synovial fluid* is increased in amount, usually to a moderate degree, rarely to excess. The fluid is usually watery and somewhat turbid, or it may be purulent.

Several gross types of joint disease are described. The commonest, in which the disease is of slow progress, and not very virulent, is known as *chronic tuberculous arthritis*. The *fungating* or *granulating form* is rarer, and occurs where the disease is somewhat more severe and rapid. The striking feature is great swelling of the synovial membrane, which protrudes into all parts of the joint as a soft, congested, spongy mass like granulation tissue. The *fibrous form* is a relatively mild, chronic type of the disease. Usually the joint is distended by watery turbid fluid, and when this is present in excess the term *hydrarthrosis* may be



FIG. 96. Tuberculosis of the elbow with superadded septic infection. The articular cartilage has been destroyed, and the exposed bone is decalcified and spongy. Around the joint are numerous outgrowths of new bone, a result of the superadded infection.  
(Museum of Royal College of Surgeons of Edinburgh)

applied. Multiple loose bodies of the "rice grain" fibrous type, are not uncommon. *Acute tuberculous synovitis* is a rare form, in which the disease runs a rapid acute course, like that of acute suppurative arthritis, for which it is liable to be mistaken.

#### Tuberculosis of Special Bones and Joints

**Tuberculosis of the Vertebrae (Pott's disease)** The spine is the commonest site for bone tuberculosis, and one of the most unfavourable,



FIG. 97 Tuberculosis of the thoracic-lumbar spine with bony union in acute angular kyphosis

(Museum of Royal College of Surgeons of Edinburgh)

for the spinal column is subject to so many strains in weight bearing and is so deeply placed that the earliest manifestations are obscure, complete immobilization is difficult to obtain, and postural deformities with secondary complications are common. Spinal disease is commonest in children, especially in those under five years, but may occur at any age. In adults the prognosis is usually grave.

The vertebrae of the lower thoracic and the upper lumbar regions, especially the last three thoracic and the first and second lumbar, are most liable to the disease, though no part is exempt. The susceptibility is generally attributed to great range of mobility as well as a considerable

amount of weight bearing in the lower thoracic and upper lumbar regions

As a rule two adjoining vertebrae are affected occasionally three or four. Rarely there are two unrelated foci at different levels.

In children the earliest lesion generally lies in the centre of the body of the vertebra, in adults not infrequently the tuberculous process begins under the periosteum on the anterior surface. Rarely it lies in the vertebral body close to the intervertebral fibro cartilage, and more rarely still in the spine, laminae or transverse processes. It is said that the usual localization of the disease to the centre of the vertebral body depends upon the anatomical distribution of blood vessels, for this part is supplied by the principal nutrient artery, a small branch of the posterior spinal artery, whereas the upper, low and anterior surfaces have a different blood supply. In adults a greater portion of the blood reaches the surface of the vertebral body, by branches from the cervical, intercostal, or lumbar arteries.

The progress of the disease may be greatly modified and aggravated by the occurrence of collapse of the body of the affected vertebra. Such collapse is an incident of some importance, for it may lead to complicating factors. (1) mechanical deformity of the spinal column, (2) dissemination of pus and tuberculous products into neighbouring tissues, and (3) involvement of the spinal cord.

(1) The deformity is usually simple kyphosis but sometimes a certain degree of scoliosis is added. The extent of the deformity varies greatly in different parts of the column, in the cervical spine the roots of the transverse processes lie almost directly lateral to the vertebral bodies, and tend to prevent or minimize deformity, in the lumbar region the column is so broad and deep and its ligaments and cartilages are so firmly attached, that deformity is rarely more than a diminution of the normal lordosis, but in its thoracic part the column is weak and the pedicles of the vertebrae lie well behind the vertebral bodies, and consequently the deformity is often great. The deformity may be a gradual bend, but often there is an acute angulation or gibbus.

The effects of the kyphosis may be severe. When the angle is in the upper thoracic region the sternum is depressed and the whole thorax flattened, when in the lower thoracic region the thorax is pushed forwards and compressed from above down, and in either case there is interference with expansion of the chest and considerable displacement of the heart and great vessels.

(2) Dissemination of tuberculous products from the collapsing bone leads to the formation of a cold abscess. At first the abscess lies closely adjoining the diseased bone, limited anteriorly by the prevertebral fascia, and it may spread beyond these confines in various directions according to the anatomical planes in the affected part. In the neck an abscess may pass anteriorly into the pharynx, or laterally to the skin of the posterior triangle, or it may track downwards into the mediastinum. In the thorax an abscess may occupy the mediastinum, or point at the surface or pass behind the diaphragm. In the lumbar region the abscess usually enters the psoas sheath and spreads to the iliac fossa, the pelvis or the groin.

(3) Involvement of the spinal cord (Pott's paraplegia) occurs in

approximately 10% of subjects of spinal caries. It may have grave consequences, and is responsible for death in about 30% of cases.

As the anterior part of the theca and cord are usually implicated in the first instance the paralysis is generally of a dissociated spastic type. It may recover quickly under appropriate treatment. In a number of instances paralysis advances progressively, either gradually or rapidly during weeks or months until it is almost total or permanent, and is often associated with loss of sphincteric control and urinary infection and for contractures and bed sores.

The mechanism underlying the paralysis is not alike in all cases. In the past onset of paraplegia has been attributed to venous congestion and oedema of the meninges and cord and possibly pachymeningitis, followed later by devitalization of a segment of the cord due to endarteritis. As the dura mater is very resistant to infection and constitutes a very effective barrier to extension of the tuberculous process it is doubtful if this view is any longer tenable. It is more likely that local pressure effects from various causes are responsible. This belief is supported by recent observations made during decompression operations on the spinal canal: they demonstrate that a variety of mechanical causes may be responsible for pressure. They are specially obvious when paralysis is of rapid onset and progression. The commonest causes of pressure are (alone or combined)—a displaced and partly destroyed intervertebral disc, a bony sequestrum, caseous collections or an abscess and in some the reconstituted and sclerosed bone of the internal gibbus. Spectacular relief may follow removal of the mechanical pressure.

**Tuberculosis of the Atlas and Epistropheus** This condition presents such distinctive features as merit separate consideration. Here the disease affects the articulations between the occipital bone and the atlas and between the atlas and epistropheus as well as the bones themselves. The joint cartilages are extensively destroyed, and parts of the bones, *e.g.*, the odontoid process may undergo sequestration. There is a special tendency for the atlas to be displaced forwards on the epistropheus. If this occurs suddenly death results immediately from impingement on the cord but if the movement is very gradual, considerable displacement may do no harm. Caries of the upper cervical vertebra may give rise to a chronic form of retropharyngeal abscess.

**Tuberculosis of the Hip Joint** Like most forms of joint tuberculosis that at the hip occurs most commonly in childhood. It arises most often between the ages of three and six years, and is progressively less frequent at later ages. In adults, tuberculosis of the hip more often represents recrudescence of an old standing disease than a fresh infection.

The infection may be primarily osseous or synovial.

The commonest bone focus is at the femoral metaphysis near the inferior aspect of the neck of the femur (the so called Babcock's triangle). At this point the disease is intra articular, and the infection may spread directly from the bone to the synovial membrane, or it may perforate the epiphyseal cartilage, invade the head of the femur, and erupt at the articular surface.



Less often the disease starts in the innominate bone close to the triradiate cartilage. From thence the disease spreads directly into the joint in the region of the pad of fat. It may spread also through the pelvic bone and lead to abscess formation within the pelvis.

In some cases there is no initial bone focus, and the infection is primarily synovial. Radiological examination at an early stage shows some increase in density of the peri articular soft tissues, but no other abnormality. Later, diffuse decalcification of both the femur and the acetabulum is a marked feature and the joint outline becomes indistinct or quite unrecognizable. There is little fluid distension of the joint, but cold abscesses in the peri articular soft tissues occur in nearly 50% of cases.

The articular cartilages are eroded, and the adjacent bone may be infected. The upper part of the head of the femur and the upper posterior part of the acetabulum undergo greatest destruction at this stage, for these parts are subject to the greatest pressure, particularly if, as often happens, the joint be flexed and adducted. The head of the femur may become greatly deformed whilst the acetabulum is deepened and enlarged upwards and backwards the so called "wandering acetabulum."



FIG. 98. Tuberculosis of the hip joint. The articular cartilages have been destroyed and the bones eroded and the femur has assumed a pronounced adduction deformity. The presence of much new bone which forms numerous marginal osteophytes indicates that a superadded septic infection had occurred.

(Museum of Royal College of Surgeons of Edinburgh.)

The process of healing in tuberculosis of the hip joint is necessarily slow. In cases in which the diagnosis has been established beyond doubt, complete healing with restitution of full movement is extremely rare. In the majority of cases, the disease persists in a quiescent state during many years, and is liable to recrudescence. Movement at the joint remains greatly impaired, owing to deformity of the articular surfaces and fibrosis of the peri articular soft tissues. Ankylosis when it occurs is always of a fibrous nature, unless there has been superadded pyogenic infection.

**Tuberculosis of the Sacro-iliac Joint.** Sacro-iliac tuberculosis is relatively uncommon. It differs from other forms of bone and joint

tuberculosis is occurring mainly in adults, generally between the ages of twenty and thirty years. It is rare in children. It may be the only apparent focus of tuberculosis, but more often active disease in the lungs coexists, and the health is gravely impaired.

Sacro-iliac tuberculosis is almost invariably osseous in origin. It generally starts in the sacrum and spreads thence to the sacro-iliac joint and to the ilium. Not infrequently, the lumbosacral articulation is also involved in the extensive destruction of bones.

Development of cold abscesses is an important feature of the disease and indeed, may provide the first sign of its presence. An

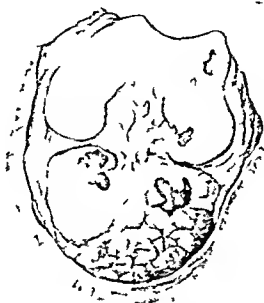


FIG. 92. Tuberculosis of the knee. The articular cartilages over both tibial condyles and the medial femoral condyle have been eroded and destroyed. A large pannus of diseased synovial membrane covers the medial condyle of the tibia.

(By courtesy of Prof J. W. S. Eschleket.)

abscess forms usually immediately to one side of the joint posteriorly, less often in the iliac fossa and inguinal or femoral region. There may be extension through the gluteal foramina, but extension to the ischio-rectal fossa is exceedingly rare.

**Tuberculosis of the knee joint.** The knee is one of the commonest sites of tuberculous arthritis. It is most often affected in childhood and early adult life, but the disease is by no means rare in old age, when it may assume a very acute form. The infection is blood borne, and in the majority of cases arises in a concealed glandular focus, much less often from an active pulmonary lesion.

Pathologically, there are two fairly distinct types of arthritis (1) synovial and (2) osteo-arthritis.

(1) The *synovialis* is commonest in elukhood. The synovial membrane is thick and gelatinous and coated with opaque nodules or tubercles. Microscopically, the lining epithelium is greatly thickened and the supporting fibrous tissue is oedematous and increased in amount and may show degenerative changes and caseation. A characteristic feature is hypertrophy of the peri-synovial fat especially around the suprapatellar pouch and the back of the joint. In many cases fringes—papillary or nodular—project from the synovial membrane and may fill the entire joint space. In almost all instances there is a considerable effusion of clear or straw coloured fluid, which may be loculated.

The synovial type of disease usually pursues a very chronic course, and, under favourable conditions shows a pronounced tendency to resolution, often without more than slight loss of movement of the joint. In severe cases caseation with cold abscess formation may occur.

(2) The *osteo arthritic* variety is characterized by destructive changes in the cartilage and the subjacent bone. In most cases the joint infection is secondary to eruption of caseating foci in the epiphyses. Such foci are more common in the femoral than tibial condyles, they are rare in the patella but may be confined to it. Occasionally at the lower end of the femur the disease is of a very massive type involving the diaphysis as well as the epiphysis. The disease may reach the joint at the reflection of the synovial membrane or at any part of the articular surface. Subchondral infiltration of the bones may lead to extensive necrosis of the cartilage, which may become loose and detached. The synovial membrane usually shares in the disease and may become extensively adherent to the ulcerated cartilage. Subluxation of the joint is a common occurrence.

In the *osteo arthritic* type of tuberculosis the joint may be greatly disorganized. Healing is usually very protracted and, even in favourable cases fibrous or osseous ankylosis is the usual result. It is in this variety, especially in adults that operative measures may be needed to shorten the course of the disease and to secure ankylosis.

**Tuberculosis of the Ankle Joint.** Involvement of this joint is usually the result of disease in the talus or of the lower end of the tibia or fibula. The disease is characterized by thickening of the synovial membrane and often by the formation of cold abscesses which erupts behind the lateral malleolus.

**Tuberculosis of the Shoulder.** At the shoulder the disease usually begins in the head of the humerus, and the disease is commonest in adult life, not infrequently in association with pulmonary tuberculosis. In many cases the arthritis is of a very chronic type and associated with organization and fibrosis of the tuberculous exudate (*caries sicca*). The cartilage of the head of the humerus is usually destroyed, and the glenoid fossa may be involved in disease or altered in contour by pressure.

**Tuberculosis of the Wrist.** At the wrist one of the carpal bones is usually affected first, especially the *os capitatum*. From here the infection travels readily to the synovial membrane and to the other bones of the wrist. In young subjects the disease may lead to gross

disorganization of the carpus and wrist joint, but in adults it is often more chronic and may culminate in fibro-osseous ankylosis.

**Tuberculous Dactylitis (spina ventosa)** This condition, nowadays uncommon, occurs mostly in children before the age of ten years. Either phalanges, metacarpals or metatarsals are affected and sometimes the disease is multiple and bilateral. In the foot the first metatarsal is most frequently affected. The earliest focus lies near the mid-point of the diaphysis—a localization attributable to the disposition of the nutrient artery, which breaks up into fine branches immediately it enters the bone. As the tuberculous degeneration progresses the periosteum of the diaphysis is raised and a shell of new bone develops; its fusiform outline is determined by the relatively firm attachment of the ligaments at the extremity of the bone. When abscess formation and superadded infection occur the pathological appearances of the bone resemble those of acute or chronic osteomyelitis. Growth in the long axis is usually interrupted or inhibited and the affected bone becomes short and barrel shaped.

**Tuberculosis of the Bones of the Skull and Face** The flat bones of the skull may be attacked by tuberculosis in childhood and in adolescence. The disease now is extremely rare. The temporal and frontal bones are those most often involved and the parietal and occipital bones only rarely. The disease begins as a localized focus in the diploe in which it may spread widely without much evidence on the exterior. At the site of disease the bone is rarefied, until finally the outer table is perforated and small light sequestra may result. On the inner table the dura mater is thickened by protective granulations.

The facial bones are occasionally affected by tuberculosis. The bone attacked most often is the zygoma in its maxillary process, the disease usually terminates in the formation of an abscess which by rupture results in a sinus situated near the lower margin of the orbit.

**Tuberculosis of the Ribs.** The ribs are liable to infection in adults more often than in children. Disease at this site is common in association with other tuberculous lesions. The infection usually begins in the neighbourhood of the costo-chondral junctions which correspond to the metaphyses in long bones. The rib is thickened and an ovoid elastic swelling may develop in the soft tissues. Abscesses arising from a tuberculous focus may track for a considerable distance before reaching the surface. Permanent healing is unlikely unless the underlying bone disease is eradicated or as in chronic cases superadded infection is overcome by removal of the ramifications of the infected sinus.

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## CHAPTER IX

### DISEASES OF JOINTS

HEALTHY joints perform their function so unobtrusively that their mechanical perfection is often not realized yet upon their smooth action depends the whole system of locomotion. Stiffness or pain even in a single joint may impede the movements of the whole body.

From their delicacy of structure and precision of movement, and from the constant stresses to which they are subject, joints are readily disabled. A joint may be incapacitated by influences which affect its interior (intra articular lesions) or from changes affecting the structures around it (peri articular lesions).

Acute diseases of joints are rare, a fortunate circumstance for their effects are often grave, but chronic diseases are extremely common. Indeed, a deforming arthritis is one of the most usual causes of chronic disability in adults and joint tuberculosis is frequent in children.

The proper working of a joint depends upon many factors among which are the free and properly co-ordinated movement of its muscles, the alignment of its bones and the integrity of its ligaments but most of all upon the condition of its bearing surface, the articular cartilage and upon its lubrication.

The cartilage, which is of hyaline type is about 3 mm thick. It is smooth, hard and highly polished and provides an ideal bearing or gliding surface.

The nutrition of articular cartilage is a problem of some interest, for the cartilage itself is entirely avascular yet nourishment must be essential for its vitality. Almost a hundred years ago Toynebee showed that in the bone deep to the cartilage there is a rich plexus of blood vessels and it seems likely that this forms the chief source of nourishment, which no doubt reaches the cartilage by a process of imbibition. Since the blood supply is most copious near the margins of the cartilage this part when irritated frequently proliferates, e.g., in osteo arthritis, whereas the central part of the cartilage is less adequately nourished and is more liable to degeneration. If a small fragment of cartilage is set free in a joint it may live and actually grow, and it must therefore be assumed that cartilage can absorb nourishment from the synovial fluid but since in health the synovial fluid has a very low protein content its nutritive value must be small.

Repair in cartilage is a very slow process for cartilage cells have little proliferative power. A wound of the cartilage is always repaired by fibrous tissue and for this reason damage to the cartilage, whether from injury or disease may lead to serious interference with joint function and often to fibrous ankylosis.

#### ACUTE PYOGENIC ARTHRITIS

Infection may reach a joint either (1) directly from an open wound, a compound dislocation, a local abscess or osteomyelitis or

the blood stream from a distant focus. The latter variety will be considered in more detail here.

The organisms responsible for acute arthritis are usually streptococci, staphylococci or pneumococci. In most cases the arthritis occurs as a complication of septicæmia, occasionally the joint lesion provides the sole evidence that organisms have been circulating in the blood stream. Not infrequently infection is derived from the throat, or from suppurative processes elsewhere in the body, such as a whitlow or puerperal endometritis. The hip joint is most often affected. The severity of the arthritis varies greatly and is determined by the virulence of the organisms. Staphylococci generally lead to such gross pathological changes in the joint as effectively prevent functional recovery, whereas streptococci may cause either a fulminating or a relatively mild subacute attack.

The synovial membrane becomes greatly swollen and congested and from œdema assumes a soft, almost jelly like consistency. Coincidentally the joint becomes distended with fluid at first of watery consistency but containing pus cells and fibrinous flakes, later purulent.

The cartilage loses the glisten of health and becomes undermined so that portions of it may become detached leaving the bone exposed and bare. The soft parts are infiltrated with inflammatory products and become softened and stretched. Escape of the purulent effusion leads to abscesses, which develop in the soft tissues and burrow in various directions. The bone abutting on the joint may undergo absorption and permit subluxation or dislocation of the joint.

Acute pyogenic arthritis may cause much pain and great constitutional reaction. In the course of septicæmia or pyæmia, however, joint involvement may be masked by the general infection, little disorganization of the joint may result.

When the infection is due to pneumococcal septicæmia the joint affection is usually of a mild and transient character.

### Typhoid Arthritis

A joint may be affected in typhoid fever at any stage of the disease. The hip is the joint most often involved and the infecting organism may be *B. typhosus* alone or mixed with *B. coli* or others. The arthritis may run a mild or severe course with or without suppuration and permanent disability may result.

*Scarlet fever*, *measles* and other zymotic diseases may also be complicated by arthritis, which is usually of mild type and non-suppurative. In *acute rheumatism* arthritis is, of course, often one of the most obvious features. These diseases are seldom of surgical significance.

### Gonococcal Arthritis

It is said that infection of joints occurs in from 2% to 5% of cases of gonorrhœa. Men are affected most often but women and even infants are not exempt. The primary focus of the disease in the great majority of cases lies in the urethra, prostate or seminal vesicles, but arthritis may occasionally complicate vulvo-vaginitis or gonorrhœal ophthalmia.



Involvement of the joints results from infection by gonococci borne in the blood stream, but it is rarely possible to demonstrate the organisms in fluid withdrawn from the joint, and for diagnosis reliance must be placed on such circumstantial evidence as recognition of the primary focus, demonstration of changes in the blood by complement fixation tests, and the effect of treatment.

Often only one joint, and that commonly the knee, is affected, but sometimes there are several especially the elbow, wrist, ankle, the joints of the fingers and the temporo-mandibular joint, occasionally the joints of the vertebral column are involved. The joint infection usually appears about three weeks after the onset of the primary lesion, but it may arise at a much later stage, when there remains only a hidden focus in the prostate, and the only sign that persists is merely slight "gleet." The intensity of the arthritis bears no relation to the extent and severity of the original infection, but in general the earlier its onset after the urethritis the more intense its effects. Apart from the arthritis there may be other evidence of infection, e.g., tendon sheathitis, bursae and aponeuroses. Rarely endocarditis, pleurisy or meningitis occur.

The intensity of the joint disease varies greatly, and there may be a transient effusion that is hardly recognizable or a severe lesion that causes much suffering, and great and permanent deformity. There is a definite tendency for the arthritis to recur with every exacerbation or fresh attack of gonorrhoea.

The following principal types are recognized.

(1) **Acute Gonococcal Arthritis.** In this type the virulence of the infection is great and its effects are correspondingly severe. A large joint such as the knee or elbow is commonly involved. The onset of the synovitis is rapid, with pain and constitutional symptoms. The joint becomes distended with turbid fluid, and there is considerable inflammatory change in the periarticular tissues. The disease may subside after a short acute phase, but often resolution is imperfect and the joint movements remain limited by fibrous periarticular adhesions.

Occasionally the joint fills with pus, there are acute inflammatory changes in the synovial membrane, the cartilages undergo destruction, and abscesses may form in the soft tissues. This suppurative type is generally due to secondary infection with pyogenic organisms.

(2) **Chronic Gonococcal Arthritis.** This is much more common than the acute affection. It occurs in two forms—the dry form and the hydropic form. The dry form of chronic gonococcal arthritis is usually polyarticular in distribution. The infection is of low virulence, and the disease is not acute but it is apt to persist for a long time and to cause great disability. Most often the wrists and the small joints of the hands are affected or the disease may attack one or more larger joints. The onset is insidious, with pain and stiffness of the joint and redness of the skin. The synovial membrane and periarticular soft tissues are infiltrated with inflammatory cells and are oedematous, but there is little or no increase of fluid in the joint. The disease may subside completely, but very commonly fibrosis occurs, both in the joint and in the soft parts, and as a result stiffness persists or increases.

Actual fibrous ankylosis may occur, often with severe contraction deformities. This type of disease bears a close resemblance to the polyarticular form of chronic rheumatoid arthritis, for which it may be mistaken.

The *hydropic form* of chronic gonococcal arthritis may involve one or more of the joints, usually large joints, such as the knees, which gradually become distended with serous or sero-fibrinous fluid. There is little or no inflammatory reaction around the joint and there are no constitutional symptoms. Movements of the joint are relatively painless and comparatively unrestricted, except by the mere presence of articular effusion. Usually the disturbance subsides but relapses are apt to occur.

### SYPHILITIC ARTHRITIS

Syphilis, unlike tuberculosis, rarely affects joints, and syphilitic arthritis is generally regarded as a very uncommon condition. Those who have made a special study of the disease, however, claim that it is not really so infrequent, and it is possible that many cases go unrecognized, or simulate rheumatoid arthritis.

In acquired syphilis the joints may be affected at any period after infection has reached the blood stream. In the secondary stage the lesions are usually of mild character. Transient pains in the joints (arthralgia) are not uncommon at the time of the skin rashes, and it is possible that these indicate a fleeting affection of the synovial membrane. Sometimes in the secondary stage there is a painless distension of the joint by clear fluid (syphilitic hydrarthrosis). It is usually transient, but may persist for long periods. The knee joint is especially liable to be affected, often bilaterally.

In the late secondary or early tertiary stages a plastic form of syphilitic arthritis may occur. Usually it is monoarticular, and the knee, elbow or mid tarsal joint is involved. Sometimes, however, it is polyarticular, and may attack the carpus and the small joints of the fingers. In its pathological features it sometimes resembles arthritis deformans, for which it may be mistaken.

The joint is swollen by œdema of the soft tissues rather than by an intra-articular accumulation of fluid. What fluid is present is turbid and thick, containing great numbers of lymphocytes, and the fluid gives a strongly positive Wassermann reaction. The synovial membrane is greatly thickened and infiltrated with lymphocytes, and the extra articular soft tissues may show a "white swelling" not dissimilar to that of tuberculosis. The underlying cause of the disease is confirmed by the prompt response to treatment by specific drugs.

In tertiary syphilis and in inherited syphilis there may occur a gummatous arthritis. Two forms of this are described (Axhausen), the *synovial* and the *osseous* forms, according to the primary site of the lesion. In either case there is great thickening of the synovial membrane and in excess of fluid collects in the joint. The cartilage may be eroded <sup>in gonorrhea</sup> regular, and there may be a gummatous osteitis in the adjacent <sup>are not</sup> of cases. In inherited syphilis the same types of joint lesion may occur, and may oc

may be bilateral. They occur most often in the knees, and commonly arise about puberty. In addition, the joints may be involved by spread of the disease from the neighbouring epiphyses (see Syphilitic Osteochondritis, p. 128).

### ARTHRITIS DEFORMANS

It seems likely that this is a medley of diseases rather than an entity, and includes all those chronic affections of joints for which no specific cause is at present known. Only comparatively recently have the articular lesions of rheumatism, gout and gonorrhoea been differentiated, and probably in the future further segregation may be possible.

The subject is confused by a baffling terminology, the result of different views in regard to the ætiology. Some of the names are variously applied to the whole disease or to any of its separate parts, and none is universally acceptable. The nomenclature employed here is the one at present in most general use, "arthritis deformans" is used as a generic term only.

At present the evidence clearly warrants the recognition of two principal sub-groups, typically quite distinct but linked by intermediate or "mixed" forms —

(1) Rheumatoid arthritis (synovial or proliferative type, chronic infective arthritis)

(2) Osteo-arthritis (chondro osseous or degenerative type)

(3) Intermediate or mixed forms

### RHEUMATOID ARTHRITIS

This disease bears no recognizable relationship to rheumatic fever or other rheumatic affections and the title "rheumatoid" is only justified by common usage. Rheumatoid arthritis is a polyarticular affection, often bilateral and symmetrical, most commonly involving the metacarpophalangeal and proximal interphalangeal joints of the hands and the smaller joints generally. The wrist, ankle, shoulder and the temporo-mandibular joints are also subject to the disease, though to a less extent. The disease affects women three or four times more often than men. It occurs at any age, but usually in adults of less than forty years.

**The Pathological Process.** The onset of the disease may be marked by an acute or subacute phase, or the progress may be insidious throughout. The joints become swollen and tender, fixed by muscular spasm and painful on the slightest movement, and this state may continue for weeks or months. Later fibrosis sets in, with restriction of the movements and often with much crippling from contractures.

The course of the disease is that of a subacute or chronic inflammation, the main effects of which fall upon the synovial membrane and other soft tissues. The cartilage and bone are also affected, but usually as a secondary process. The synovial membrane is invaded by lymphocytes and plasma cells, and becomes congested and œdematous. It is greatly swollen, and projects into the joint as red, proliferating, spongy masses, which fill up every available space in the recesses of the joint and creep as a web or pannus over the surface of the articular

cartilage, often eroding it. When, in the later stages, the inflammatory process subsides there is much proliferation of fibrous tissue, which fixes bare portions of the bony surfaces and leads to severe contraction deformities.

As in many situations where inflammation has subsided, there is a great tendency to the accumulation of adipose tissue in the synovial fringes, such a condition, if extensive, is known as *lipoma arborescens*. Occasionally also small islands of cartilage or even of bone may appear in the fringes, though this is more characteristic of osteo-arthritis.

The synovial fluid is usually reduced below the normal quantity. The cartilage becomes atrophied and thin and the joint space narrowed. The bone becomes rarefied, partly on account of the inflammatory process and partly from disuse. When a severe contraction deformity exists, part of the bone may become absorbed, and allow of subluxation. Intra articular ligaments suffer when the bone is affected, and become eroded and disintegrated. The long head of the biceps, for instance, as it passes through the shoulder joint may disappear completely. The articular capsule and extra articular soft tissue are much affected being at first swollen and oedematous, and giving the enlarged joint a fusiform shape. In the later stages fibrosis in these tissues, together with similar changes in the joint, leads to the fixation and deformity which form such a disabling feature of the disease. The skin over the joint becomes thin and bluish white, its surface dry and shiny.

**Ætiology.** Many theories have been advanced in regard to the ætiology of rheumatoid arthritis and still it remains unsolved. Briefly, the main groups of theories may be classified as the non infective and the infective. In the former group are such factors as congenital predisposition and endocrine disturbances, of which it is impossible to say more than that they remain unproved. It has been suggested that an important part is played by disorders of metabolism and delay in the removal of ingested glucose from the blood, faulty elimination of sulphur, and abnormal phosphorus metabolism have all been suggested. This very multiplicity, however, precludes conviction.

There can be no doubt that in a large proportion of cases the disease is closely related to some infective or toxic condition. Not infrequently there is a history that the onset of the joint disease has been preceded by an exacerbation of some infective focus in the upper air passages, in the throat, or elsewhere, and a temporary "lull" in the joint disease with subsequent improvement is a common result when such a focus is removed. Moreover, in adults occasionally, and in children more often, there are other signs of chronic infection, such as sallow complexion, enlargement of lymph glands, and occasional pyrexia. In children also the spleen may be enlarged (Still's disease). It is interesting to note that often there is an absence of hydrochloric acid from the gastric contents and that the bacterial flora of the stomach and upper intestine is greatly altered and increased. It is possible that toxic absorption from this source plays some part in the ætiology.

Bacteriological examination of the joints is usually negative, a few workers have claimed to be able to isolate streptococci, diplococci or other organisms with regularity, but confirmation of such findings is

lacking. More probably the joints are affected by toxins derived from distant septic foci. It has been suggested that the affection is an allergic one, and that from repeated exposure to allergic influence the joints are rendered hypersensitive to small doses of toxin.

### OSTEO-ARTHRITIS

This is an age-old affliction of mankind. Ruffer has described many interesting specimens obtained from the tombs of ancient Egypt, including examples of spondylitis and of osteo arthritis of the hip, shoulder and other joints. Osteo arthritis has even been found in skeletons 6000 years old. Lower animals are also subject to the disease, both in captivity and in their natural haunts.

In typical instances osteo arthritis differs greatly from rheumatoid arthritis. It affects adults and old people, especially males, it mainly affects one joint at first (though others may be involved to a less degree), and it affects articular cartilage and bone principally, synovial membrane to a less obvious extent. This general statement, however, is subject to qualification, for intermediate forms are common.

Osteo arthritis affects the knee most often, then the hip (*malum coxae senilis*), the metacarpophalangeal joint of the thumb, and the corresponding joint of the great toe. In elderly people a mild, though sometimes disabling, form of osteo arthritis is often seen in the joints of the fingers. The joints, ligaments and cartilages of the vertebral column may be affected and constitute the condition known as spondylitis deformans which will be described separately (*see p. 297*).

**Morbid Anatomy.** The pathological process affects cartilage and bone primarily and principally, the synovial membrane and other soft tissues only at a later stage. Cartilage and bone undergo changes which are both degenerative in nature but also to a great extent proliferative.

The changes in the joint are different at the centre from those at the periphery. The central part of the articular cartilage is comparatively ill nourished and, moreover, bears the brunt of the body weight or other forces, whereas the peripheral portion is adequately nourished and little subject to pressure. Consequently the changes in the central area are principally degenerative, those at the periphery chiefly proliferative.

The central part of the cartilage is affected first. It undergoes degenerative changes whereby it becomes dull and velvet and of soft consistency. Microscopically, the earliest change is in the smooth hyaline matrix of the cartilage, which becomes fibrillated and frayed. The cartilage cells lose their regular arrangement, and they become swollen and eventually disappear. Sometimes whilst the greater portion of the cartilage is worn away small areas remain unaffected and form smooth rounded eminences on the articular surfaces—*epi articular eechondroses*.

At the periphery of the joint surface the cartilage proliferates and forms large irregular masses—*peri articular eechondroses* or *chondrophytes*—which may fringe the entire joint like an extension of its articular surface or may flank it like irregular buttresses or may project in polypoid fashion. Such outgrowths usually become ossified.

and may then be called *chondro osteophytes*. Sometimes they form a complete collar round the joint and interfere greatly with movement.

When the cartilage is worn away, the bone at the joint surface becomes exposed, and often undergoes a curious change known as *eburnation*, whereby parts of its surface become dense, smooth and shiny like porcelain or ivory. In hinge joints such as the elbow or knee the to and fro gliding movement may give rise to an alternation of cartilage-covered ridges and grooves. The bone is decalcified, porous and light, and near the joint it is sometimes replaced by areas of fibrous tissue in which small cysts may develop. Softening of the bone may lead to secondary deformities, as at the hip, where *coxa vara* may occur with shortening and apparent broadening of the neck.

and sometimes extensive resorption of the head.

The synovial membrane is affected at a relatively late stage. It is thickened, and from its surface project numerous processes, which may be fine, delicate and filamentous, or coarse and pedunculated (*synovial villi*). These are very liable to be nipped between the joint surfaces, when temporary increase of fluid in the joint results, with exacerbation of pain and disability. Masses of cartilage may grow in the synovial fringes (*synovial chondromata*) from small islands of cartilage cells normally present. They may attain large size and may become calcified or even in part ossified. In other cases masses of fat accumulate in the synovial fringes and project into the joint (*lipoma arborescens*).

Loose bodies are of very frequent occurrence in osteo-arthritis. The majority of the loose bodies arise from detached synovial fringes, and hence may be composed entirely of fibrous tissue or may contain fat or cartilage. Usually



FIG. 100. Osteo-arthritis of the knee. A specimen obtained post mortem from an elderly person who had not complained of symptoms referred to the joint. Numerous fibro-fatty villous masses project from the synovial membrane. Note that the suprapatellar bursa is unaffected.

(Museum of Royal College of Surgeons of Edinburgh.)

in the last variety some calcification is present, and often true bone. Other bodies arise from the detachment of portions of periarticular or epiauticular chondrophytes (see p. 200).

*Heberden's nodes* are small rounded bony outgrowths which arise from the bones of the fingers and project under the skin. They are common in osteoarthritis and are usually multiple and symmetrical. They lie close to one of the interphalangeal joints, commonly the terminal ones. Often they lead to deviation of the terminal part of the finger and to flexion or extension deformity. Usually they cause little disability, but occasionally they give rise to limitation of movement.

**Pathogenesis of Osteo-Arthritis** The most noteworthy feature in the pathology of osteoarthritis lies in the close association of degenerative and proliferative changes—the articular cartilage over the centre of the joint surface is softened and worn away, whereas that at the periphery is stimulated to grow. It seems most satisfactory to attribute this differential effect to the fact that the central part of the cartilage is poorly nourished and moreover is subject to the constant pressure of the opposed articular surface, whereas the peripheral parts of the cartilage are better nourished and are subject only to intermittent pressure.

In a large proportion of cases there is evidence that trauma plays an important part in the development of the arthritis. Thus a mobile medial meniscus or a loose body may in the course of time lead to arthritis. In other cases there are occupational strains, or stresses from faulty statics, as at the knee joint after malunited fracture, or in knock knee, or at the first joint of the great toe in flat foot. It cannot be accepted, however, that trauma alone can cause osteoarthritis, it merely determines the involvement of certain joints in persons who for other reasons are susceptible to the disease.

It seems possible that in some cases the predisposing factor is a chronic low grade toxæmia derived from distant septic foci, such as are frequently present. Others have upheld the view that the general predisposing factor is some derangement of metabolism or of the internal secretions for osteoarthritis commonly occurs at the climacteric and may be associated with hypothyroidism or other endocrine affections.

### NEUROPATHIC DISEASE OF JOINTS (Charcot's Joints)

In 1868 Charcot described a peculiar joint affection that follows diseases of the central nervous system. In 80% of cases this neuropathic



FIG. 101 Osteo-arthritis of the shoulder. Note the eburnation of the head of the humerus and the osteophytes at the margin of the articular surface.

(Department of Surgery, University of Edinburgh.)

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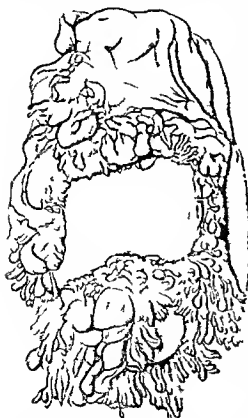


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(Museum of Royal College of Surgeons of Edinburgh.)

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FIG. 101 Osteoarthritis of the shoulder. Note the erosion of the head of the humerus and the osteophytes at the margin of the articular surface.

(Department of Surgery, University of Edinburgh)

"arthritis" is due to *tabes dorsalis*, in most of the remainder it is due to *syringomyelia*, but it may rarely follow cerebral diplegia, myelitis, and other lesions of the brain cord, and peripheral nerves. In *tabes*, since the nerve lesion affects the lower part of the spinal cord, the

joints affected are almost always those of the lower extremity. Most often the knee is involved, less frequently the hip or the ankle. Occasionally two joints are involved, either simultaneously or in succession. In *syringomyelia*, since the cervical part of the spinal cord is affected, the joints of the upper extremity are most liable to involvement. The arthropathy of *syringomyelia* almost invariably affects the shoulder.

"Charcot's disease" is a term generally restricted to the joint manifestation of *tabes*, but this differs from that of *syringomyelia* in no fundamental feature except in causation. "Charcot's disease" is a parasyphilitic or meta-syphilitic affection, which is not due to any direct effect upon the joint by spirochetes or their toxins, but is secondary to a loss of trophic influence or some other change resulting from the nerve lesion. It has been estimated that "Charcot's joints" occur in about 3% of patients suffering from *tabes*. The joint lesion may arise at any period of the disease, even at an early stage so rendering its recognition difficult.

**Appearance of the Affected Joint** The pathological changes are remarkable in that there is at the same time extremely gross destruction of bone and articular cartilage, and often equally excessive irregular new formation around the joint. The whole process develops with rapidity and with entire absence of pain.

The first morbid change appears to consist in decalcification and resorption of the articular ends of the bones, and occasionally



FIG 104. Tabetic arthropathy of the knee. The lateral condyle of the femur and the head of the tibia have been eroded. From the proximal end of the tibia a large shelf of new bone projects forwards.

(Department of Surgery, University of Edinburgh.)

this can be recognized in radiograms before there is any visible affection of the joint itself. As a result of some degenerative process the articular ends of the bone become soft and friable, and in this state, favoured by the absence of pain, the bone crumbles as a result of weight bearing and friction. The articular end of the bone is rapidly eroded, often with the formation of irregular grooves and ridges, and eventually large portions of it may disappear. Often the joint contains massive loose bodies. At the hip, the head and neck of the femur may vanish entirely, as though by the action of some corrosive agent (see Fig 103).

At the knee the ends of the tibia or femur may be destroyed, or one condyle may disappear while its fellow remains relatively unaffected.

Coincident with the degenerative changes there is irregular production of cartilage and bone, so that chondrophytes and osteophytes appear at the margins of the joints and in the substance of the capsule, forming irregular friable masses, which may be detached as loose bodies.

The synovial membrane shares in the destructive changes and



FIG. 103. *Tabetic arthropathy of the hip (Charcot's joint).* Note the gross destruction of bone and its extensive regeneration. The original acetabulum has disappeared completely, and a greatly enlarged joint cavity is surrounded by an irregular rim of new bone. There are several large masses of loose bone, which occupied the synovial membrane and the peri-articular tissues.

(Museum of Royal College of Surgeons of Edinburgh.)

becomes softened, disorganized, and infiltrated with granulation tissue. The capsule, intra-articular ligaments, and tendons may disintegrate and the peri-articular tissues are swollen with oedema far beyond the joint, and the overlying skin may be erythematous and congested.

As a result of the bone deformities and of the laxity of the articular capsule the joint often becomes dislocated. The soft parts stretch greatly and the joint forms a thick voluminous bag, and may even open into bursæ or the neighbouring joints. Thus at the ankle the joint

may ultimately include the whole of the talus and other tarsal bones. The interior of the cavity is lined by a rough granulating membrane from which project polypoidal chondro-osseous masses. The fluid of the joint is viscid, yellow, or often blood stained.

**Types of the Disease.** Three pathological types have been described, according to the relative extent of the destructive and regenerative changes. The commonest form of the disease, seen most often in the knee in tabes, and characterized by much new bone formation, has been termed the *hypertrophic type*. The form seen in the shoulder, or less often in the hip, in which new formation is not evident and destruction predominates, has been called *atrophic* and the rare form in which both destruction and new formation occur in but limited degree, and in which the changes resemble those of arthritis deformans, is known as "*osteo-arthritis*". It is evident that these so-called "types" are merely variations from the average, and the classification has a clinical rather than a pathological value. It seems probable that the extent and character of the changes depend to some degree upon the amount of movement that the joint has been allowed.

**The Cause of the Disease.** The cause of neuropathic joint disease, the relationship of destructive changes on the one hand and of new formation on the other, and the dependence of the whole process upon some perverted nerve influence, form a study of particular interest from the standpoint of the physiology of bone formation.

It is abundantly clear that the fundamental process is one of degeneration or destruction. New bone formation is a later process, and probably is attributable to the liberation of a vast amount of calcium which readily precipitates in any available medium in the vicinity.

It is not clear how disease of the central nervous system produces these effects, for removal of trophic influences alone is insufficient to account for them. It seems probable that the repeated trauma permitted by the absence of pain is an important factor, for Eloesser has shown experimentally that after section of the posterior nerve roots to a limb, joint changes only occur if repeated injury is inflicted.

## LOOSE BODIES IN JOINTS

Loose bodies in joints vary greatly in their number, nature, and mode of origin. They may be solitary or present in large numbers, even up to 100, they may be composed of cartilage, bone, fibro-fatty tissue, or fibrin, and they may arise as a consequence of either injury or disease. For convenience they may be classified as they occur in healthy or in diseased joints.

**Loose Bodies in Healthy Joints.** The most striking example of a loose body occurring in a healthy joint is the so-called "classical" loose body in the knee. Such a body is commonly oval in shape and about the size of an almond, and it is almost always single. It results from detachment of a portion of an articular surface, usually a portion near the posterior aspect of one of the femoral condyles, or sometimes

the back of the patella. Consequently one surface of the loose body is usually convex, smooth, shiny and covered by hyaline cartilage, whilst the other surface, originally the deep aspect, is flat or of irregular contour.

Loose bodies of this type almost always affect males in early adult life, and the cause of the detachment is not yet clearly understood. According to Paget, the cause was a "quiet necrosis" of the subjacent bone, presumably resulting from the action of some toxin, and a somewhat similar process has been suggested by Koenig, who gave it the name "osteochondritis dissecans." It seems more probable, however, that the essential feature is thrombosis resulting from trauma, which leads to impairment of the blood supply of a limited area of the articular surface and to slow separation of the devitalized portion. Often there is a history of a previous injury to the joint, and even when such a history is unobtainable there may be presumed to have been a minor injury or perhaps repeated small stresses.

Once set free in the joint such a loose body is apt to become impacted between the articular surfaces and to give rise to pain, locking and effusion of fluid. Subsequently the recurring trauma may predispose to chronic arthritis.

It is an interesting fact that these loose bodies once set free continue to live, and indeed the cartilage cells may actually proliferate so that eventually every aspect of the body is covered by cartilage. It appears that the nourishment required for survival and growth is derived from the synovial fluid.

*Other loose bodies* occurring in normal joints include such bodies as fragments of bone set free by fractures and portions of intra articular cartilages detached by trauma. Loose bodies of both these types most commonly occur in the knee joint, less often at the elbow. The tibial spine may sustain fracture, and the medial semilunar cartilage is often detached in part or completely, as a result of injury.

Occasionally loose bodies composed of newly formed cartilage derived from the synovial membrane (synovial chondromatosis) occur in healthy joints, but they are far more common in joints affected by chronic arthritis.

**Loose Bodies in Diseased Joints.** Loose bodies may occur in many forms of joint disease, but they are most common in tuberculous arthritis, osteo arthritis and neuropathic arthritis. They occur most frequently in the knee, shoulder and elbow (in that order of frequency), and are rare in other joints.

*Fibrinous loose bodies* most commonly occur in tuberculous joints. They are small and oval or somewhat elongated like melon seeds or grains of rice, and they resemble the loose bodies found in bursae and tendon sheaths. They are of firm consistency but not hard, and consequently they do not tend to become impacted between the articular surfaces. They are usually present in large numbers and there may be as many as a hundred. Occasionally a fibrinous loose body is solitary, and is then apt to attain greater size.

Microscopic examination shows that the bodies are laminated but

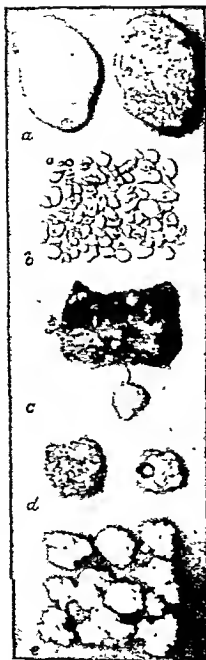


FIG. 104 Loose bodies from joints. (a) A "classical" loose body, with the convex surface smooth, the other rough; (b) multiple fibrous bodies of melon-seed or rice-grain type; (c) synovial membrane with multiple cartilaginous bodies attached; (d) loose bodies from a case of osteo-arthritis; (e) multiple cartilaginous loose bodies, probably derived from synovial chondromata.

(Department of Surgery, University of Edinburgh.)

have no cellular structure, and they appear to be composed principally of inspissated fibrin. Doubtless they owe their shape to the pill-rolling effect of the joint movements.

*Fibro-fatty loose bodies* most commonly occur in joints affected by osteo-arthritis or rheumatoid arthritis, but may occur in tuberculous and neuropathic joint disease. They are derived from hypertrophied fringes of synovial membrane, which project into the joint and become polypoidal and pedunculated. Sometimes the bodies lie entirely free in the joint, but more often some remain attached by delicate pedicles. They are liable to be nipped between the articular surfaces and thus cause recurrent pain and effusion.

*Bony and cartilaginous loose bodies* are most common in osteo-arthritis, but they may occur in other joint affections.

In osteo-arthritis the marginal outgrowths or chondro-osteophytes may project towards the joint space, and one or more of them may be detached and set free in the joint. Such pathological loose bodies contain small areas of bone but are composed mainly of fibro-cartilage, which serves to distinguish them from separated portions of the articular surfaces, which are composed of hyaline cartilage.

Other chondro-osseous loose bodies are derived from the synovial membrane (synovial chondromata). Many years ago K  lliker showed that the synovial membrane normally contains islets of cartilage cells, and under certain circumstances

these cells proliferate to form cartilaginous masses of considerable size. Such chondromata are usually associated with osteo arthritis but they may occur in the absence of any obvious joint disease. They may project superficially and be palpable as hard lobulated masses closely related to the articular ends of the bones, or they may protrude into the joint and ultimately be set free. Synovial chondromata are frequently multiple and usually do not attain a diameter of more than a centimetre. Occasionally the greater part of the inner aspect of the synovial membrane is studded with small masses of cartilage. Sometimes there is a single chondroma in relation to an otherwise normal joint, and rarely it may attain large size, for example, the one shown in Fig 105 which measured 8 cm in its long axis.

**Cysts of the Menisci of the Knee Joint.** Cyst formation in the menisci of the knee joint is of fairly frequent occurrence and the lateral meniscus is affected about six times more often than the medial. The cysts involve the anterior third or half of the meniscus and especially its periphery. There may be one or more large cysts which may attain a centimetre in diameter, they are separated by fibro cartilaginous septa from a variable number of smaller cysts. The cysts contain gelatinous material. The lining membrane is smooth and glistening, and microscopically is found usually to consist of a single layer of flattened cells like endothelium.



FIG 105 Synovial chondroma measuring 8 cm in the long axis removed from the lateral aspect of the knee of a woman aged sixty-two years. The knee joint showed slight osteo arthritic changes.

(Department of Surgery, University of Edinburgh.)

The aetiology is not fully understood. In nearly all cases injury has preceded the development of the cysts, and although it may have occurred several months or even years previously, its importance cannot be ignored. But trauma seems to be only an exciting factor, because the cysts lack haemorrhagic characters. Their clear contents suggest that they may result from degeneration of areas of devitalized fibro cartilage, probably the result of injury of tissue of normally poor vitality, a belief which is substantiated by the finding of endarteritis in the tissues adjacent to the cysts.

Some regard the cysts as distensions of synovial islet spaces present in the menisci, and assert that the lining is endothelial. The more common belief is that the cellular lining of the cysts is derived from the cells of the cartilage.

**Congenital Disc-shaped Lateral Meniscus.** The embryonic disc

pattern of the lateral meniscus of the knee occasionally persists. In outline it may be circular, quadrilateral, or simply unusually broad at its interior horn (comma shaped). The importance of the abnormality is that it predisposes the cartilage to injury, and too may be responsible for a peculiar painless snapping noise in the outer part of the knee. The 'snap' occurs at about 20° short of full flexion and full extension, and at the same time a momentary check in joint movement occurs and the tibia and femur separate slightly and then fall together again. Both the 'snap' and the altered gliding of the joint surfaces are accounted for by a transverse ridge at the anterior part of the cartilage which in extremes of movement must be surmounted by the femoral condyle.

### SPONTANEOUS OR PATHOLOGICAL DISLOCATION OF JOINTS

A joint may be dislocated as a result of disease of the muscles which support it or govern its movements, or from diseases that affect its component parts. Usually there is a combination of factors varying in different joints. The joints in which pathological dislocation has been most frequently observed are the hip, the knee, and the occipito atlantoid articulation.

*At the hip* pathological dislocation is more common than the traumatic and the dislocation is always dorsal. Arthritis septic or tuberculous is the commonest predisposing cause but occasionally paralysis of the abductors and extensors of the hip, such as follows poliomyelitis or birth injuries has been responsible. Probably in both varieties trauma of such a degree that would not affect a normally constituted joint determines the actual dislocation. The prolonged assumption of the attitude of flexion and adduction, in which position the head of the femur is least supported by the acetabulum, favours dislocation and the stretched capsular ligaments and eroded articular surfaces render the obstacles still fewer. If the dislocation is overlooked the muscles and ligaments become shortened in adaptation to the altered position of the femur. In old standing cases the limb is shortened and assumes an attitude of flexion and adduction, and movements are restricted and painful. A false joint may develop on the dorsum of the above the acetabulum.

Dislocation due to muscular paralysis usually follows the adoption of faulty attitude from unopposed muscle action in paralysis of the abductor and extensor muscles of the hip, or it may follow contraction of the flexor and adductor muscles in spastic paraplegia.

*At the knee*, spontaneous dislocation is usually due to arthritis, septic, tuberculous or neuropathic. The dislocation is a posterior displacement of the tibia and is attributable to inadequate support of the posterior aspect of the joint whereby the tibia falls backwards out of line with the articular surface of the femur.

Pathological dislocation of the knee is exhibited in an exaggerated form in tabetic arthropathy. From loss of the articular surfaces and



the destruction of intra articular ligaments the joint may be moved in almost any direction without pain

*At the atlanto-occipital or atlanto-epistropheic joint* forward displacement of the skull or of the atlas may occur, as a result of tuberculous caries or from the effects of regional hyperæmia. If the atlas be suddenly displaced forward the dens may impinge on the medulla or the upper part of the spinal cord and cause sudden death. Considerable displacement of the vertebræ may occur without the cord becoming compressed provided the dislocation is gradual. In some cases there is merely torticollis deformity with marked fixation and great pain on attempted movement

## HABITUAL OR RECURRENT DISLOCATION OF JOINTS

Repeated dislocation from comparatively slight causes is especially apt to occur at the shoulder and at the temporo mandibular joint

At the shoulder, mobility and wide range of movement are obtained at the expense of stability, and the joint gains relatively slight support from its bony surfaces or capsule, but owes its security principally to the reinforcement of the muscles around it. The glenoid ligament (labrum glenoidale), which consists of a strong ring of dense fibrous tissue, serves to deepen the joint and probably increases its stability

The usual traumatic dislocation occurs by indirect violence and the head of the humerus escapes through a rupture of the antero inferior part of the capsule between the tendons of the subscapularis and the triceps. When reduced, sound healing of the capsule occurs and recurrence of dislocation is very unusual. The recurring type of dislocation follows a different kind of injury—an impact from the head of the humerus on the antero inferior part of the glenoid ligament resulting usually from a fall on the back of the shoulder or on the elbow when the arm is moderately extended. Athletes and epileptics are very commonly the victims of such severe injury. Recurrence of the dislocation, which may occur from very slight violence, is due to shearing off of the anterior margin of the glenoid ligament and its failure to reattach itself

Recurrent dislocation of the temporo mandibular joint is a relatively rare condition, it may be unilateral or bilateral. The tendency to repeated dislocation has its origin in a former acute dislocation which has produced stretching or rupture of the ligaments and muscles of the joint, and especially the external pterygoid muscle. In some instances the meniscus is unduly lax or is torn, and this predisposes to redislocation

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## CHAPTER X

### DISEASES OF MUSCLES, TENDON SHEATHS AND BURSÆ

#### CONTRACTURE OF MUSCLES

CONTRACTURE of muscles is a frequent accompaniment and sometimes a cause of deformities. Shortening may result from any of the following causes: (1) prenatal lesions of muscle, causing congenital deformity, (2) prolonged approximation of the points of attachment of the muscles, for example, in old dislocations, or after fixation in positions of flexion, (3) weakness or paralysis of opposing muscle groups, for example, in poliomyelitis, or after peripheral nerve injury, (4) disease in the related joint, especially rheumatoid arthritis and gonococcal arthritis, (5) disease or injury of muscles, with subsequent fibrosis and contracture such as follows fracture, osteomyelitis, etc.

The character of the deformity depends upon the nature and extent of the underlying lesion. Sometimes, especially when resulting from nerve injuries, the deformity is very characteristic, for example, the "main en griffe" of ulnar nerve paralysis and the drop foot following paralysis of its extensor and evertor muscles.

Three special types of muscular contracture—prenatal muscular dystrophy, torticollis, and Volkmann's ischæmic contracture—require special mention.

#### PRENATAL MUSCULAR DYSTROPHY

Many congenital skeletal deformities, such as *congenital high scapula*, *bilateral club hand and club foot* (arthrogryposis multiplex congenita), *congenital genu recurvatum* and *congenital angulation of the tibia*, are believed to result from muscular dystrophy developing fairly late in intra uterine life. Histological researches in these and similar conditions suggest that the underlying defect is some variety of prenatal myodysplasia, in which developing muscles either fail to reach full structural maturity, or, if fully developed, tend to degenerate because they are unable to maintain themselves in a state of high differentiation. No lesion of the peripheral nerves has been discovered.

*Congenital high scapula* is associated with absence of the lower part of the trapezius, and the upper part together with the rhomboid muscles is the seat of fibrous infiltration. In addition, there is usually evidence of widespread disturbance of development of the mesodermic structures of the neck, in the form of congenital kyphosis, crania- or spina bifida, and irregular segmentation of the cervical part of the vertebral column. Probably, as was suggested by Middleton, the high position of the scapula and its failure to descend are due not so

much to muscular anomaly as to irregularity of development of the mesoblastic components of the cervico dorsal segment of the trunk and the upper limb buds. The muscles of the shoulder girdle merely share in the disturbance of development.

*Arthrogryposis multiplex congenita* is a rare deformity in which there is bilateral clubbing of the hands and/or of the feet. The muscles of the limbs are wasted and joint movement is restricted. When the lower extremity is affected congenital dislocation of the hip joint is frequently present and is of such a type that reduction is more than usually difficult or impossible.

The counterpart of arthrogryposis has been observed frequently in lambs, and is regarded as a simple autosomal recessive. In the human subject hereditary factors appear to be absent. The microscopic appearance of the affected muscles is the same in man and animals and consists of fibro fatty degeneration, similar to that observed in the muscular dystrophies of later life. Apparently, the muscle degeneration occurs late in intra uterine life and affects muscle fibres which are already fully differentiated. Once started the degeneration progresses rapidly but ceases at birth.

From the surgical standpoint, it is worthy of note that the club foot differs from the more familiar congenital talipes in that there is absence of muscular power and a greater difficulty in effecting reduction, but after correction there is less tendency to recurrence of deformity.

*Congenital genu recurvatum* (congenital dislocation of the knee) may be unilateral or bilateral, it is frequently associated with other limb developments such as club foot and congenital dislocation of the hip. The knee joint is fixed in hyperextension, which can be increased slightly by manipulation, but flexion is restrained by the elastic resistance of the stretched hamstring muscles. Anteriorly the plane of the joint is marked by transverse creases in the skin, posteriorly the prominence of the femoral condyles may be detected. The patella is usually undeveloped or may be absent. The cause of the deformity is contracture of the quadriceps muscle, the result of antenatal fibro fatty degeneration.

*Congenital angulation of the tibia* is characterised by anterior kyphotic angulation of the tibia at the junction of its middle and distal third and is associated with extreme and fixed talipes equinus. The limb as a whole is short, particularly the part below the knee. Other abnormalities of development frequently co exist.

Although there are no demonstrable microscopic changes in the calf muscles, it is thought that the deformity results from failure of the final stages of muscular development, because the finer degrees of muscle dystrophy, short of disintegration, cannot be identified.

The contraction of the affected muscles leads to bending and angulation of the cartilaginous tibia.

### CONGENITAL TORTICOLLIS (Wry-neck)

Congenital torticollis results from fibrosis and consequent contracture of the sterno mastoid muscle. Both sternal and clavicular heads are

affected and in well-established cases they stand out as tight bands. The shortening leads to restriction of growth of all the other soft tissues in the affected part of the neck, including the deep fascia, the sheath of the great vessels, and the scalene muscles.

The contracture causes limitation of the movements of rotation and elevation of the head, and the head is flexed, bent towards the affected side, and rotated towards the opposite side. In many cases there is asymmetry of the face and skull, on the affected side the face is small, and the frontal tuberosity is flat, on the opposite side the occipital bone bulges. Owing to excessive shortness of the fibrosed muscle the mastoid process on the affected side is abnormally large, and an exostosis may develop at its clavicular attachment. Thoracic-cervical scoliosis often develops.

Formerly, torticollis was attributed to an injury sustained at birth and was regarded as the end result of a "sternomastoid tumour," a spindle shaped mass of young fibrous tissue sometimes found a week or two after birth and believed to be due to partial rupture of the muscle during the process of parturition.

This theory, however, fails to account for the fact that the contracture may occasionally be present in fully developed form at birth nor for the common association with congenital asymmetry of the skull. It seems more probable that the deformity is due to congenital aplasia.

### VOLKMANN'S ISCHÆMIC CONTRACTURE

This stubborn form of contracture generally affects the flexor muscles of the hand and forearm and causes considerable deformity and disability. Less often (see below) it affects the muscles of the calf and foot. It is an occasional (and sometimes unavoidable) complication of fractures and dislocations in the region of the elbow, less often of more distal fractures. It is commonest between the ages of five and fifteen years, the period when these fractures are most often sustained. In rare instances the contracture has developed after injury to the soft tissues of the arm, the prolonged application of a tourniquet, and embolism of the brachial artery.

At the onset of the contracture, which may be evident a few hours after the injury, there is usually burning pain in the hand and forearm and great agony follows attempts to extend the fingers. Swelling and blueness (rarely pallor) of the fingers are of special significance. The radial pulse is much reduced in volume or imperceptible. When the contracture is fully developed the wrist is flexed, the fingers are extended at the metacarpo-phalangeal joints and flexed at the interphalangeal joints. Since the tendons are free from adhesions the fingers can be straightened after flexing the wrist. The general nutrition of the limb is often impaired, and the hand is cold and blue.

In established cases the appearance of the affected muscles is quite characteristic. They are indurated and surrounded by a dense fibrous sheath, and the muscle substance is replaced by a yellowish green homogeneous substance which cuts with difficulty. The outstanding

*microscopic change is an irregularly distributed mass necrosis of muscle fibres with fibrous proliferation around the dead muscle bundles. In places groups of fibres survive and may show hypertrophy.*

Volkmann's contracture is now known to be due to interference with the arterial blood supply to the muscles. In some cases the brachial artery is compressed directly by a displaced fragment of bone or by external pressure from splints or bandages. In other cases the artery or its branches are obliterated by spasm secondary to the trauma. Yet again they may be compressed by a hematoma confined beneath the deep fascia.

Recently it has been shown that a similar contracture may affect the muscles of the calf and foot. If the site of vascular occlusion is the popliteal artery (the result, for example, of pressure by a tight plaster cast) all the muscles are involved. More often, a single group of muscles or even a single muscle belly is affected as a result of a less extensive ischaemia due to the pressure of a hematoma.

Volkmann's contracture may be accompanied by motor or sensory paralysis. Formerly it was assumed that the paralysis is due to incorporation of nerve trunks in the scar tissue but more probably there is a coincident nerve lesion due, like the muscle necrosis, to ischaemia.

A similar *traumatic ischaemia of nerves* may occur independently and may result from thrombosis or compression or spasm of the main artery or from pressure caused by a hematoma beneath the deep fascia. The paralysis involves all the nerves of the part and affects light touch and joint sensitivity more than deep pressure or pin prick. It starts at the extremity, spreads centripetally and assumes a glove or stocking distribution. When it is due to swelling beneath the deep fascia nerves with a long superficial course may escape.

## RUPTURE OF MUSCLES AND TENDONS

Despite the severe strains to which muscles may be subjected, rupture is not a common injury. Subcutaneous rupture is commonest in adults or elderly subjects following unexpected violent contraction, (sometimes by the opposing group of muscles). Diminished tone or *hyaline degeneration*, such as may follow a debilitating illness, is sometimes a predisposing factor. The muscle usually ruptures where its fibres converge on tendinous prolongation, but the tear may affect the belly of the muscle or the tendon itself.

The gap created by rupture of a muscle is first filled by blood, then fibrin is deposited, and later granulation tissue bridges the space. Replacement by scar tissue finally occurs, but there is never union of muscle to muscle or regeneration of its fibres however accurate apposition may have been. The ultimate function of the muscle so far as power and motion are concerned, is likely to be normal provided scar tissue does not bind it to adjacent fixed structures, such as fascia and bone. In some situations the fibrous tissue at the site of repair may become attenuated and, in the abdominal wall, may predispose to hernia.

Severance of a tendon is followed by separation of its ends, and the degree of retraction depends on the position of the part and the state of contraction of the related muscle at the time of the rupture. The process of repair is on the same lines as in muscle by fibrous tissue replacement of the intervening blood clot and fluid exudate. Provided the gap is not excessive, and adhesion of the tendon to adjacent structures can be overcome, the natural process of fibrous contraction effects a secure approximation.

The commonest sites for rupture of muscles (or tendons) are—the rectus femoris or one or all components of the quadriceps, the tendo calcaneus the tendons or muscle *bodies* of the biceps brachii, and the extensor tendons of the thumb and fingers, especially the index and ring. In rare circumstances the rectus abdominis muscle undergoes rupture, especially below the umbilicus, where its posterior sheath is deficient. Sometimes there is a coincident rupture of the deep epigastric vessels and a diffuse hæmatoma develops. Sometimes the rupture has been caused by direct violence, usually, however, it follows slight exertion, especially in subjects debilitated from such illnesses as typhoid, influenza and pneumonia. It has been observed during pregnancy and parturition and following the muscle cramps of tetanus. The practical importance of the condition is that it simulates intra abdominal disease such as appendicitis, cholecystitis and strangulated hernia.

### OSSIFICATION IN MUSCLES AND TENDONS

Ossification in relation to muscles is usually the outcome of injury, either contusion fracture, or dislocation. The resulting mass of bone is usually known as *traumatic osteoma* a designation which justifiably replaces the older term *traumatic myositis ossificans*.

Localized ossification is common in the muscles and tendons of those subject to osteoarthritis. The bone is usually in the form of spikes, sometimes known as *false exostoses*, which are often continuous with the roughnesses to which the muscles secure attachment. Similar bone formation may occur in association with neuropathic arthritis, particularly of the knee.

**Traumatic Osteoma.** A traumatic osteoma resulting from a simple contusion and unassociated with a fracture has been observed most often in connexion with the quadriceps femoris following a severe blow. The bone develops in a hæmatoma and is not usually apparent for five to eight weeks after injury, it is not in the muscle fibres, but between them, or in the inter muscular planes. If a radiogram of a limb is taken some weeks after a severe contusion it may be noted that, even in the absence of fracture, the bones for a distance from the point of injury show slight rarefaction. It is probable that injury to the periosteum releases lime salts for ossification to occur in the organizing hæmatoma (*see p. 116*).

Intermittent and unaccustomed strain may lead to ossification in the affected muscles or tendons. A familiar example is the keel shaped plate of bone that grows from the *linea aspera* between the tendons of the adductor longus and brevis in cavalry recruits unaccustomed to horsemanship.

Traumatic osteoma associated with fractures and dislocations has been observed most often in relation to the femur or the humerus, and at the elbow joint. The principles underlying the new bone formation are the same as those mentioned above. At the elbow joint the ossification occurs between the brachialis muscle and the shaft of the humerus, and its occurrence has sometimes been observed after forcible manipulation of a stiff joint, the new bone may lead to considerable limitation of movement, but it tends to disappear provided movement is restricted for sufficient time. If the osteoma persists it may give rise to disability by limiting the movement of the muscles or by impeding the excursion of a neighbouring joint.

**Myositis Ossificans Progressiva** Infiltration of muscles by bone is seen on an extensive scale in myositis ossificans progressiva—a rare disease in which large deposits of lime salts in bone develop in relation to muscles, aponeuroses, ligaments, and fasciæ. It affects young male subjects, seldom women. Its ætiology is not known.

The muscles affected in the early stages are those of the back and neck, especially the latissimus, trapezius, and rhomboids. At the onset of the disease there are attacks of stiff swelling and tenderness in the affected muscles which become firm and doughy.

Prior to bone formation there is hyperplasia of the intramuscular fibrous tissue and deposition of lime salts between the muscle fibres and in the intermuscular planes. The bone is of a spongy texture and is often disposed in large sheets or plaques in the interstices of the muscles. In addition, there may be large osseous projections from the vertebral spines, the ilia, and the scapulae. None of the bony masses lies free and unattached to the skeleton.

As ossification progresses, movements of the back and limbs become greatly impaired. The ribs become fixed and respiration is solely by the diaphragm. Death is due usually to pulmonary infection.

A frequent and striking coincidence in the recorded cases is congenital hallux valgus caused by imperfect development of the phalanges. A similar deformity of the thumbs is usually present.



FIG. 100. Traumatic osteoma.

(From a specimen of the Royal College of Surgeons of Edinburgh.)

## TUMOURS IN MUSCLES

Tumours in muscles are uncommon, and most of them arise from the muscle sheath or the intermuscular fibrous tissue. The commonest varieties of simple tumour are lipoma, hæmangioma, fibroma, and fibrosarcoma.

A lipoma may arise in the muscles of the shoulder girdle or of the thigh. In other situations it is rare. The tumour is soft when the muscle is relaxed, but becomes firm and hard during contraction. Difficulty in diagnosis of an intermuscular lipoma may be considerable when it is situated beneath a firm aponeurosis.

A hæmangioma is a very rare tumour in muscles. It occurs generally in young subjects, and is probably congenital. The tumour is of the cavernous type, and is localized usually in one part of the affected muscle, but occasionally the tumour is diffuse.

A muscle hæmangioma is usually soft and compressible, unless thrombosis has occurred within it. When the tumour is pulsatile it may

resemble a rapidly growing sarcoma.

**Recurrent Fibroma or Desmoid Tumour.** This is a tumour peculiar to muscle, of special interest because it has the microscopic character of a simple neoplasm, yet it has no capsule, tends to infiltrate widely and is very apt to recur after removal. It does not form metastases.

The tumour occurs most often in the rectus abdominis muscle but is seen also in the deltoid, the gluteal muscles and occasionally elsewhere. In the rectus

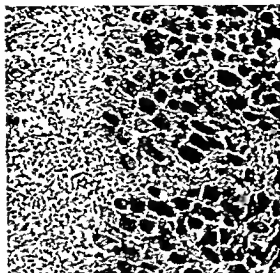


FIG 107 Fibroma (desmoid tumour) of the rectus sheath. The tumour is very cellular, and has infiltrated between the fibres of the muscle

(Museum of Royal College of Surgeons Edinburgh.)

muscle it is seen most often in parous women, and has been attributed to rupture of the muscle fibres during parturition, while in other cases there may be a history of a blow.

When small the tumour is pinkish-white in colour, and is so hard that it creaks when cut. Its cut surface has a tendon like appearance, hence the old term "desmoid tumour". When large the tumour is softer, and it may show mucoid degeneration. On microscopic examination the tumour has the appearance of a fairly cellular fibroma with cells arranged in bundles or whorls. The stroma is scanty and the blood vessels are small but well formed. Characteristically it infiltrates the muscle fibres, which in consequence lose their striation and undergo degeneration.

Microscopic examination shows that the invading cells extend a long way beyond the visible margin of the growth. It is for this reason that recurrence is so common, even after a wide local resection.



Progress is slow but in the course of years the tumour spreads widely. Thus from the rectus muscle it may eventually implicate the muscle sheath, the peritoneum and even the pubic periosteum, while from the deltoid muscle it may spread to the pectorals and thus to the chest wall.

## TENOSYNOVITIS

Tendon sheaths have the same structure as the synovial membranes of joints and are affected by the same diseases. They are liable to become inflamed (tenosynovitis) as a result of injury, and to become infected by pyogenic organisms, gonococci, and tubercle bacilli.

Well developed tendon sheaths are found only at the wrist, in the fingers, and at the ankle joint, and these, therefore, are the usual situations of tenosynovitis.

**Traumatic Tenosynovitis.** Traumatic tenosynovitis (tenosynovitis crepitans) sometimes follows a severe strain or excessive use of a particular group of tendons. As only a small number of people who submit their tendons to undue strain develop tenosynovitis, it may be presumed that some constitutional factor must be superadded.

In this variety of tenosynovitis the opposed surfaces of the tendon sheath are covered with fibrinous lymph which imparts a crepitant sensation when the tendons move. It may be accompanied by considerable subcutaneous oedema. There may be an effusion of rusty fluid into the sheath, but it is merely large in amount. The tendons most often affected are the extensors of the fingers and those of the toes.

**Infective Tenosynovitis.** Infective tenosynovitis may be of two varieties: (1) acute, and (2) chronic.

(1) **Acute tenosynovitis** may be toxic in origin or due to pyogenic organisms from a septic lesion in the proximity of one of the large tendon sheaths or to gonococci carried in the blood.

**Pyogenic or suppurative tenosynovitis (thecal whitlow)** occurs in characteristic form in association with septic infections of the hand. The infection is usually due to streptococci, less often staphylococci. The sheaths of the flexor tendons of the fingers and of the wrist are more often affected than those of the extensors. Infection may arise in any of several ways: not infrequently infection of the sheath follows directly from a prick on the volar surface of the finger, especially at the proximal interphalangeal crease where the sheath is most superficial. In other instances infection is carried by the lymph vessels from an adjacent cellulitis, or it is conveyed from a subcutaneous whitlow either by natural extension or as a result of a careless incision.

When the tendon sheaths of the little finger or the thumb are affected, extension to the common flexor sheath is apt to occur owing to their direct communication with it. In the case of the other fingers such extension is uncommon, for after pus has burst through the proximal end of the sheath, it passes into the middle palmar space or to the thenar space rather than to the common flexor sheath.

When a tendon sheath is infected it becomes hyperæmic and thickened, its inner surface covered with purulent lymph and the

sheath distended with pus. If the pus is not evacuated, the tendons, deprived of their blood supply, may slough, and infection may extend to the adjacent bones and joints. The formation of fibrous adhesions usually gives rise to permanent contracture of the fingers.

Gonococcal tenosynovitis may occur as a complication of gonorrhoea in either sex. It may begin at any stage of the infection, but is commonest about the second to the third week of the disease. It has been known to occur in infancy as a result of gonococcal ophthalmia.

Gonococcal tenosynovitis usually occurs simultaneously with infections of the joints. The tendon sheaths at the wrist and ankle are those most often affected, the extensors more often than the flexors.

In the acute stage of the tenosynovitis, gonococci can often be demonstrated in the fluid obtained by puncture of the sheath.

The severity of the tenosynovitis varies. In mild cases there is effusion of serous fluid into the affected sheath, associated with pain and impairment of movement. In more severe cases there are considerable redness of the skin and oedema of the subcutaneous tissues. Only rarely does suppuration occur, and if it does the tendons do not tend to slough as in other pyogenic varieties of tenosynovitis. After gonococcal tenosynovitis adhesions may form in the sheath and lead to stiffness.

(2) Chronic tenosynovitis, if non-traumatic is generally tuberculous. The commonest site is the large flexor sheath at the wrist, less often the sheaths of the extensor and peroneal tendons at the ankle joint are involved. The disease affects young adults and is frequently the only manifestation of active tuberculosis (compound palmar ganglion).

The pathological features are observed in most characteristic form at the common flexor sheath at the wrist. Sometimes the extensor and the digital sheaths are affected in addition or independently. The disease may present itself in various forms which are probably accounted for by variations in its duration and by varying local and general resistance. In its simplest and early form a serous exudate is present, later granulation tissue and "rice bodies" appear, and, finally, in the severer forms extensive caseation may occur.

When inspected at operation the deep fascia is found to be tense and the underlying sheath is no longer white and glistening but yellowish grey, greyish red or purple. It is distended with straw-coloured fluid and the tendons may be thickened and matted by vascular granulation tissue which renders them dull and lustreless. At a later stage there may be loculation of the fluid or the sheath may be partially obliterated by fibrous tissue or by "rice bodies". In advanced cases the fluid is replaced by caseous or gelatinous material. At first the tendons though thickened as a result of proliferation of their visceral sheaths are healthy, but in severer cases there may be destruction of a single tendon or groups of tendons. The median nerve, which is intimately related to the common flexor sheath, is often swollen as a result of oedema of its sheath but its fibres are not affected.

The progress of the disease is very variable, in some cases fibrous tissue formation may limit the disease, in others it may assume a chronic hypertrophic form. Sometimes extensive caseation may lead to perforation of the sheath and a cold abscess.

Tuberculous tenosynovitis at the wrist leads to stiffness and weakness of the fingers. Pain of a burning character in the distribution of the median nerve is sometimes present. Tenosynovitis, when complicated by osseous disease or active lesions elsewhere, is treated most suitably by excision of the diseased tissue, and the degree of recovery depends on the extent to which there may have been destruction of tendons.

**Tumours of Tendon Sheaths** A miscellaneous variety of tumours arise from tendon sheaths (as from bursæ and joints). Such tumours usually solitary, may be fibrous, myxomatous, or even cartilaginous, and are subject to various forms of degeneration. The tumour, usually nodular is seldom larger than a cherry and is of slow growth and in all respects benign. It affects usually the tendon sheaths of the wrist and fingers less often those of the foot. It is commonest in young and middle aged adults, and may cause pain and disability.

The tumour is encapsuled and grows outwards rather than towards the tendon sheath. It may be grey or pink or altered by degeneration or hemorrhage. The histology of these tumours is variable. Fibrous, giant cell, and xanthomatous forms are described and these particular types are often combined with cystic, myxomatous or lipid or other changes.

The origin of synovial tumours is not fully ascertained. It is more than likely that synovial surfaces are derived not as endothelium but as modified connective tissue specialized to form a pavement endothelial like surface. The non committal title "*Synovoma*" has been adopted to embrace the varied histological types occurring in tendon sheaths, bursæ and joints.

In all but a few instances a *synovoma* is simple and easily enucleated from its capsule. Sarcomatous types—fibro—spindle cell, etc., are known, but are very rare. Their malignant character is usually obvious from the outset.

## DISEASES OF BURSÆ

Bursæ minimise friction, and are usually present where tendons pass over bony surfaces or where the superficial fascia and skin cover a bony prominence. In structure bursæ resemble the synovial capsules of joints and tendon sheaths, of which in some situations bursæ are merely prolongations. At sites where the skin and subcutaneous tissue are exposed to intermittent friction, abnormal bursæ may develop. Such bursæ are known as *adventitious bursæ*, and their development is often due to repeated trauma incident to particular occupations. Similarly, adventitious bursæ may develop in relation to deformities of the skeleton, especially where bony prominences are exposed to abnormal intermittent pressure, familiar examples of such bursæ are those over the head of the first metatarsal in ballux valgus (bunion), those over the tarsus in club foot, and those over the end of the bone in amputation stumps.

Bursæ are liable to many of the same forms of disease as joints and tendon sheaths, and when a bursa is in communication with a

joint it participates in any pathological condition that involves the joint

Traumatic bursitis usually results from excessive friction and pressure and occurs most often in the superficial bursae, less often, the more deeply placed bursae such as the semi membranous bursa and the subacromial bursa are affected. Traumatic bursitis is characterized by an increase of serous fluid in the bursa and thickening of its lining membrane. The process may be an acute one, and is then attended by considerable pain and disability. More often, however, the process is chronic and the bursa distends slowly with fluid (bursal hydrops).

If the inflammation does not subside, or if it relapses frequently

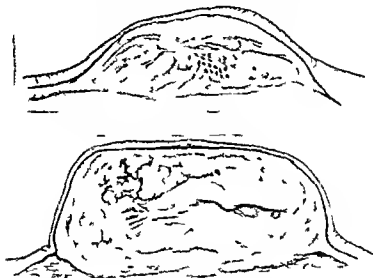


FIG 108 Bilateral chronic prepatellar bursitis in a woman aged eighty three above concentric thickening due to proliferation of fibrous tissue below large swelling due to fibrous tissue overgrowth and gelatinous degeneration

the walls of the bursa may become very thick and irregular adhesions, septa or fringes may form in its interior, or concentric thickening may ensue, resulting in a fibrous swelling (see Fig 108). Occasionally, loose bodies of the melon seed variety may develop within it.

The prepatellar bursa and the olecranon bursa are those most liable to injury and various fanciful names have been assigned to the conditions according to the occupation which was suspected to produce it for example housemaid's knee and student's elbow.

Subacromial bursitis may occur as an immediate or late sequel to injuries to the shoulder, such as a blow, a wrench or a dislocation. In the majority of cases the underlying lesion is an injury, usually rupture, of the fibres of the tendon of the supraspinatus muscle. The rupture usually takes place close to the greater tuberosity and the subsequent

retraction of the tendon (it may be far as much as 2½ inches) enlarges the gap and establishes a communication between the shoulder joint and the bursa. Probably smaller tears of the tendon, which involve only a few fibres, are quite common, and the intratendinous calcification which frequently follows may give rise to the features of traumatic subacromial bursitis.

Acute infective bursitis frequently follows abrasions and wounds, and, as superficial bursae are structurally related to the lymph vascular system, it is not uncommon in cellulitis or lymphangitis. The prepatellar and the olecranon bursae are most often affected.

In suppurative bursitis the walls of the bursa become greatly thickened, the inner surface is destroyed, and the cavity is filled with thick yellow or sanious pus. The resulting abscess may burst through the skin or track for a considerable distance in the subcutaneous tissue and lead to cellulitis. When healing occurs the bursa may be completely obliterated by fibrosis.

Gonococcal bursitis is less common than gonococcal arthritis, which it resembles very closely in its pathological features. The bursa most often affected is that at the insertion of the tendo calcaneus.

Tuberculous bursitis is uncommon. It is most apt to occur in bursae near large joints, such as the hip, shoulder and knee, and is then usually secondary to tuberculosis of these joints. Nevertheless the subacromial bursa, which does not normally communicate with any joint, may be the seat of tuberculosis in the absence of disease in the neighbouring bones or joint. Similarly, the iliopsoas bursa, situated between the psoas muscle and the capsule of the hip joint, may be affected by tubercle, as may the various bursae related to the gluteal muscles.

**Other Diseases of Bursae.** In gouty subjects chalk may be deposited in the walls of bursae. Calcareous deposits in the subacromial bursa or in the tendon of the supraspinatus muscle are common and are usually the result of trauma. Involvement in syphilis is extremely rare.

The occurrence of a giant cell tumour, cellular fibroma and fibrosarcoma (synovioma) fibroma in bursa has also been reported.

**Ganglion.** A ganglion is a cystic swelling which occurs in the neighbourhood of a joint or tendon sheath, especially at the wrist, ankle, and knee. In many instances it appears soon after a strain, in others there is no obvious cause. Ganglion is common in either sex, but more so in women than in men. Often it disappears spontaneously.

The cyst is generally unilocular, is very thin walled and contains clear, jelly like fluid. It may reach the size of a pigeon's egg. The wall of the cyst is composed of fibrous tissue which adheres lightly to the surrounding tissues. There is no endothelial lining. The mode of origin of a ganglion is uncertain. It is generally stated that it arises from a synovial sheath or a joint. Certainly at the carpus it is usually possible to demonstrate a communication between the ganglion and the interior of the wrist or intercarpal joints. Although the cyst may adhere to the tendon sheaths, a communication with them is not usually discovered.

The most likely cause of ganglion formation is mucoid degeneration

of injured capsular ligaments ; in some instances they may be extrusions of synovial membrane from nearby joints.

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## CHAPTER XI

### DISEASES OF BLOOD VESSELS

#### THROMBOPHLEBITIS

No clear distinction can be drawn between thrombosis occurring in healthy veins (phlebo thrombosis) and thrombosis associated with inflammatory changes in the wall of the vein (phlebitis)

This disease commonly affects the veins of the lower limbs and pelvis. It occurs most often as a post-operative complication or after childbirth, but it is by no means rare in patients confined to bed for any reason. Occasionally it arises in healthy persons, especially the elderly.

Post-operative Thrombophlebitis nearly always occurs in middle-aged or old patients and is most common after operations on the abdominal or pelvic organs. It usually becomes manifest a week or ten days after operation, though exceptionally it may appear as early as the third day or as late as the third week.

The thrombosis usually starts in the deep veins of the calf muscles, less often in the veins of the saphenous system or in the deep veins of the thigh or of the pelvis. At first the clot forms slowly and is white in colour, consisting of fibrin with many platelets and leucocytes, but few red cells. Later as coagulability increases there is a more rapid laying down of red clot, extending in a proximal direction. This forms a "tail" to the thrombus, which lies free in the lumen and may extend a long distance from the original site. Thus it is not uncommon to find that a white thrombus originating in the veins of the calf muscles has a red tail floating freely within the common femoral vein or even higher. Probably this red tail is in no sense a permanent clot, but increases and diminishes as phases of increased coagulation are succeeded by phases of clot lysis. It is for this reason that anti-coagulants such as heparin and dicumarol are effective, for when the coagulability of the blood is reduced the fibrinolytic substances which are normally present quickly lead to disappearance of much of the existing clot.

The local effects of thrombophlebitis vary greatly. Simple thrombosis of moderate extent may give rise only to slight oedema of the extremity. More extensive clotting of the deep veins causes marked swelling of the limb with distention of superficial vessels and blueness of the skin. If the superficial veins are thrombosed they may be palpated as tender cords. In the presence of phlebitis there is pain in the affected area, while tenderness can be elicited by direct pressure or, in the calf, by forcible dorsiflexion of the foot. In the most extreme type, which formerly was common in puerperal cases, owing to peri phlebitis with obliteration of lymphatic channels the whole limb becomes greatly swollen, dead white and painful (phlegmasia alba dolens).

The great danger of thrombophlebitis lies in the liability of the red tail of the clot to be set loose and give rise to pulmonary embolism (p 336). It is noteworthy that this complication is more apt to supervene upon a small unnoticed thrombosis than a severe phlebitis, probably because in the latter circumstance the clot is more firmly attached to the wall of the vein.

The cause of post-operative thrombophlebitis is not clearly understood but probably there are three main contributory factors. (1) The presence of tissue products set free at the site of operation. (2) mild infection. (3) venous stasis. This last factor is probably the most important.

There is evidence to suggest that sometimes the thrombosis starts in the early post-operative phase as a result of pressure on the calf muscles as the patient lies flaccid on the operation table, or the pressure of a bolster placed under the knees to maintain the semi sitting position may be a determining factor. It is noteworthy that the incidence of phlebitis can be reduced by early vigorous movement.

In the course of time as the process subsides the thrombus becomes organized by fibroblastic tissue which extends into the clot from the intima. Later the clot is recanalized and in cases of mild or moderate extent the patency of the venous pathway may be fully restored. In severe cases however some venous and lymphatic stasis may persist and give rise to chronic œdema of the limb. As a late sequel a leg ulcer of particularly resistant character may develop.

The progress of thrombophlebitis is greatly influenced by the use of anticoagulants. *Heparin* a mucosin sulphuric ester is so called because it was isolated first from the liver. Originally it was believed to exert its effect by inhibiting the activity of prothrombin. According to the view now held it is the anticoagulant normally present in the blood and its effect is to activate antithrombin. *Dicumarol* is the active agent in sweet clover disease a hemorrhagic disorder occurring in cattle fed on wet stacked clover. Its anticoagulant effect depends upon its property of inhibiting the formation of prothrombin. Unlike heparin which is transient in action and rapidly eliminated dicumarol acts slowly and its effect is prolonged and cumulative.

**Migrating Thrombophlebitis.** This condition may occur in young men and is then often associated with thrombo angitis obliterans. It has been observed occasionally in cases of deep seated malignant disease e.g. bronchial carcinoma or carcinoma of the pancreas.

The disease affects superficial veins particularly in the lower extremity and often starts in the foot or at the ankle. Occasionally it arises in the arms or trunk. The affected vein over a length of 4 cm. is palpable as an indurated tender cord while the overlying skin is swollen and inflamed. After an acute phase lasting a few weeks the local process subsides though the vein remains occluded. After an interval which may be as long as several months a similar episode occurs either close to the first or at a distance.

**Axillary Thrombosis.** Primary thrombosis of the axillary vein is a rare disease which generally occurs in healthy young men. It is usually a sequel to a minor injury or to long continued occupational stresses.



particularly such as are sustained when the arm is fully abducted above the head. Where there is no history of strain the swelling has usually been noted on waking, and it is assumed that a constrained position during sleep has been a factor.

It is thought that the vein may be damaged through being stretched, or it may be compressed by the subclavius muscle, the costocoracoid membrane or various muscle slips, which sometimes cross the floor of the axilla. Perhaps in some cases one of the valves, which are often found at this level, is ruptured.

Thrombosis of the axillary vein gives rise to venous obstruction in the limb with swelling, cyanosis and elevation of the venous pressure. Collateral channels dilate rapidly and are apparent under the skin or may be demonstrated by infra red photography.

In due course the thrombus is organized and eventually it may be partly recanalized.

## ANEURYSM

An aneurysm has been defined as "a space or sac formed by the widening or extension of the lumen of an artery, and thus containing blood or clot." It is customary to recognize *true aneurysms*, resulting from disease and bounded by the stretched out coats of the arterial wall, and *false or traumatic aneurysms*, resulting from puncture or rupture of the artery, and bounded only by condensed fibrous tissue derived from adjacent structures. There is, however, no essential difference in the morbid anatomy of the two forms, for in true aneurysms of any considerable size the sac wall rarely contains any trace of the original coats of the artery.

The predisposing cause of an aneurysm is weakening of the arterial wall, especially of its middle coat of muscle and elastic fibres, which stretch and eventually gives way under the pressure of the blood. High blood pressure is an important contributory cause, but is not a necessary one. The weakening of the arterial wall may result from developmental defects, disease or injury. Amongst diseases predisposing to aneurysm, syphilis stands foremost, because of its especial tendency to affect the middle arterial coat. Simple atheroma and arterio sclerosis may be responsible in some vessels. In some situations weakening of the media results from a chronic periarterial infection, as, for example, in arteries traversing tuberculous cavities or large peptic ulcers.

An aneurysm may be fusiform or saccular. In the saccular type the communication between artery and aneurysm may be small and remain so, unless the aneurysmal sac communicates with large adjacent arterial trunks, such as at the root of the neck. For this reason there is a great liability to recurrence after proximal ligation of the main trunk alone. The interior of the aneurysm is rough and irregular, and on it consequently the blood tends to clot. When coagulation occurs intermittently, there is a formation of laminae of various ages, the older being pale and fibrous, the more recent red and jelly like.

**Traumatic Aneurysm.** Trauma may determine the onset of an

aneurysm of a diseased artery, but the term "traumatic aneurysm" is restricted to those cases in which a healthy artery is affected. The trauma is usually from penetrating bullet or stab wounds, but occasionally from puncture by a spicule of fractured bone. Traumatic aneurysm is apt to follow lateral or traversing wounds of arteries particularly when the wound is oblique and the entrance and exit wounds are small or valvular. It never follows complete severance of an artery, an injury which permits retraction of the muscular coat and closure of the arterial wound. The arteries of the neck and extremities are commonly affected especially the carotid axillary and femoral.

The extravasated blood at first forms a simple hæmatoma in the peri arterial tissues but within a short time it becomes circumscribed and surrounded by fibrous tissue, which forms a recognizable sac, sometimes partly lined by endothelium derived from the arterial intima.

**Arterio Venous Aneurysm** In about 20% of traumatic aneurysms there is a coincident wound of the accompanying vein and this is followed immediately or subsequently by the establishment of a communication between the two vessels. Usually the artery and vein communicate directly or by means of a short wide channel (aneurysmal varix) less often the anastomosis is indirect through an intervening sac lying in the soft tissues (varicose aneurysm). Such an intervening sac is often of irregular shape and very tortuous and from the pressure of the blood within it is apt to enlarge progressively.

In the days of venesection arterio-venous aneurysms frequently occurred in the cubital fossa. Nowadays they are usually due to penetrating wounds. Occasionally an arterio-venous aneurysm occurs in the intracranial portion of the internal carotid artery following fracture of the base of the skull and gives rise to the condition of pulsating exophthalmos (*see p. 220*).

Arterio-venous aneurysms provide an interesting illustration of the adaptation of structure to function. There is a great increase in the blood flow through the artery proximal to the anastomosis and a great decrease in the blood flow through the artery distal to it. Consequently the proximal part of the artery dilates the distal part becomes contracted. The vein suddenly subjected to pressure greatly in excess of normal becomes greatly dilated and tortuous and since the pressure is not sustained but rhythmically alternating the wall of the vein undergoes hypertrophy and often attains the thickness of an artery. Proximally, the dilatation may extend even as far as the vena cava and the heart (which is hypertrophied) distally, it is checked temporarily by any valve present in the vein but later it renders the valve incompetent and extends distally. If the communication is a large one there are important effects both on the general circulation and on the state of the extremity. At the onset there is a sudden fall in blood pressure and a rise in pulse rate. As arterial blood enters the venous system the venous pressure is greatly raised and consequently the cardiac output is increased. Later as the heart hypertrophies the systolic blood pressure rises towards its former level but the diastolic pressure remains low. If the fistula is occluded the heart beat is slowed and the pulse pressure falls sharply (brady cardia reaction).

The changes in the extremities are mainly due to venous insufficiency and are similar to those following thrombophlebitis—varices oedema stasis pigmentation chronic induration cellulitis and ulceration. In a young subject the limb may undergo an increase in length. If the by pass is a large one gangrene of the extremity may occur as a result of ischæmia.

**Congenital Arterio-Venous Fistula** This rare abnormality is seen most often in an extremity occasionally within the cranium. It may be associated with angioma either of the port wine or cavernous type with neurofibromatosis or with other congenital defects.

Nearly always in the affected limb there are numerous fistulae so small as to render their identification impossible.

They may affect the major vessels or minor ones in the muscles or in the fingers or even within the bones. The increased vascularity leads to generalized overgrowth of the limb a kind of local gigantism. The whole limb may be affected or only a part for example the hand or even a single digit. Generally the disease is manifest in infancy but it may appear first during adult life. Its progress is usually slow but



FIG. 10) Congenital Arteriovenous Aneurysm

occasionally there is rapid increase in size simulating a malignant tumour. At first the enlargement affects principally the soft tissues but later the bones are increased in length owing to increased vascularity of the metaphyses.

The superficial veins become obliterated and tortuous and very numerous. The oxygen content of the venous blood approximates to that of arterial blood. The skin is hot and sweats readily. An accidental wound even of small size may cause catastrophic hæmorrhage. Sometimes extensive ulceration develops in the distal part of the extremity.

#### Aneurysms at Special Sites

**Aneurysm of the Thoracic Aorta** This is by far the commonest example of aneurysm. It is of surgical interest principally from its

into anterior and middle cerebral arteries, and the point of origin of the first large branch of the middle cerebral artery in the lateral fissure. Less often an aneurysm may arise at the origin of the ophthalmic artery, or at the origin of the anterior communicating artery. The basilar and vertebral arteries are seldom affected.

Aneurysms of the basal cerebral arteries occur in quite young subjects and even in childhood. Arteriosclerosis and syphilis take no part in their development. The adventitial and the muscular coat of the cerebral vessels are poorly developed, and local defects in the vessel walls are

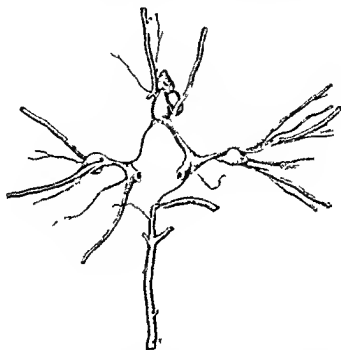


FIG 110 Aneurysms of the cerebral arteries. Three aneurysms are seen on the middle cerebral arteries and the anterior communicating artery respectively. Death resulted from hæmorrhage from the anterior aneurysm.

(By courtesy of Prof J W S Blacklock.)

common, so that even with a normal blood pressure dilatation may occur.

An aneurysm of one of the cerebral arteries may produce no effects, but rupture, leading to subarachnoid hæmorrhage, is relatively common. Its occurrence in otherwise healthy subjects under thirty years is well known. Rupture may be fatal, but more often the extravasation is localized and associated with frontal headache and an incomplete paralysis of the oculo motor nerve. When the extravasation is more widespread the signs are those of cerebral hæmorrhage, usually followed by cranial nerve palsies and focal cerebral signs. In a few instances an aneurysm may reach a large size and produce effects similar to those of an intracranial tumour.

*Aneurysm of the intracranial part of the carotid artery as it traverses*

the cavernous sinus is fairly common, especially in middle aged women. It is usually of saccular type and most often involves the anterior extremity of the vessel. In rare cases the condition is bilateral. The usual causes of arterial degeneration do not contribute to the formation of an aneurysm at this site.

The limitations of space within the cavernous sinus and the proximity of the nerve trunks which it harbours in its lateral wall, account for the somewhat dramatic onset of symptoms and the sequence of paralytic phenomena. The onset, more often abrupt than gradual, is attended by hursting neuralgic pain over one side of the head and in the eye, followed by a varying degree of ocular muscle paralysis. One or more of the branches of the semilunar ganglion—commonly the first and second—show pressure effects. The initial explosive effects are usually followed by a gradual subsidence, but significant pressure phenomena persist. In rare instances when there has been stripping of the dura mater from the middle fossa, there may be paresis of the facial nerve or even pressure on the brain stem. In established cases there may be deformation of the surrounding bone, particularly of the sphenoidal boundaries of the orbital fissure, the optic foramen and the anterior clinoid process. Concentric rings of calcification within the aneurysm are sometimes present.

*Intracranial Arterio-venous Fistula* of the internal carotid artery within the skull is due in most cases to injury, but it may arise spontaneously from rupture of a simple aneurysm into the cavernous sinus.

A large proportion of fractures of the base of the skull involve the body and the great wing of the sphenoid, so that it is not surprising that the carotid artery, which is relatively fixed in the cavernous sinus, is sometimes injured. On rare occasions the artery is injured by a traversing wound of the orbit. The wall of the artery may be torn at the time of the accident, or its coats so damaged that a communication with the sinus develops later. The nerves in the cavernous sinus may be damaged at the time of the accident or by pressure later.

The objective features of an arterio-venous aneurysm resemble those of a simple aneurysm, but, in addition, it is characteristic that the orbital and palpebral veins become dilated and "arterialized," so that pulsation may be seen in them. The eyelids often become coarse, thick, and cyanotic. Pulsation and protrusion of the eyeball is often present—*pulsating exophthalmos*. The patient is usually conscious of a continuous bruit which is very disturbing, especially at night. There is usually a notable deterioration in general health.

## HYPERTENSION

The systolic blood pressure may be raised with no concomitant rise in the diastolic pressure, for example in aortic insufficiency or when the elasticity of the great blood vessels is diminished by arteriosclerosis. The term *hypertension* is generally used, however, to describe the condition in which both the systolic and diastolic levels are raised, and indeed it is recognized that it is the diastolic blood pressure which is affected primarily and is of the greater significance.

Hypertension is due essentially to an increase in the resistance to the flow of blood at the periphery, particularly in the smaller arterioles. Two types are recognized. The term *secondary hypertension* is applied where the cause of the increased peripheral resistance is manifest, the term *primary* or *essential* or *idiopathic hypertension* is used when the underlying cause is not apparent.

Secondary hypertension is seen most commonly in association with arteriosclerosis and diffuse *glomerulo-nephritis*. Less often the renal lesion is of different type, for example *pyelo-nephritis* or *polycystic disease*. Secondary hypertension also occurs as a result of coarctation of the aorta and as a consequence of the hormonal disorders associated with diseases of the pituitary and adrenal glands. In the cases of tumours of adrenal medulla (*phaeochromocytoma*) the hypertension is variable, being due to intermittent release of excessive quantities of *adrenalin*. A special form of secondary hypertension is due to *unilateral kidney disease*, for example *pyelonephritis*, *hydronephrosis* or *calculous disease*. In some such cases removal of the affected kidney has led to cure or amelioration of the hypertension. The mechanism of this process is considered below.

*Primary or essential hypertension* is now recognized as a very common condition, and indeed it is claimed by some workers that as large a proportion as 70% or 80% of all cases of "raised blood pressure" fall initially into this category. Two types of essential hypertension are recognized, the benign and the malignant. Probably they are not to be regarded as separate states, but rather as variants of a single disease, their character depending on the age at onset and the rate of progress of the pathological process.

Benign hypertension as seen particularly in elderly persons, is of gradual onset and slow progress and comparatively mild in its clinical effects. When recognized it is usually associated with arteriosclerosis and chronic renal disease. Formerly it was assumed that in this type of case, the common "high blood pressure" of old people, the hypertension was a secondary result of the organic renal and vascular changes. The tendency at present, however, is to believe that the hypertension precedes and is the cause of these organic changes. Malignant hypertension, by contrast, occurs mainly in younger subjects, even as early as the third decade, it follows a rapid course and it may proceed to a fatal issue within a few years or even within eighteen months from the onset of the symptoms.

**Ætiology of Essential Hypertension** It is believed that this form of hypertension is due primarily to widespread vasoconstriction, affecting particularly the peripheral arterioles and that the vasoconstriction is brought about initially by sympathetic stimulation. It has long been recognized that in health a transitory hypertension occurs as a result of such emotional states as fear or excitement, or mental stress, and it seems probable that such stimuli when occurring in susceptible persons may gradually lead to permanent elevation of the blood pressure.

The importance of an inherent susceptibility is indicated by the fact that a family history is present in a considerable proportion of

cases According to Platt essential hypertension is a hereditary disorder conveyed as a mendelian dominant with a rate of expression of over 90%

The relation of renal disease to hypertension is now recognized to be of great importance It has been shown by Goldblatt that in animals hypertension occurs regularly if the blood supply to the kidney is reduced for example by applying a silver clip to the renal artery By a series of ingenious experiments Goldblatt has shown that this result is due to the production of a substance—renin—which is formed in the ischaemic kidney It is believed that renin produces its effect by actuating an angiospastic substance which gives rise to spasm of the arterioles and thus causes widespread constriction of the peripheral circulatory channels

Goldblatt's experiments give a ready explanation of the occasional cases in which hypertension occurs as a complication of unilateral renal disease Some recent observations serve to indicate that they may be well of significance in relation to the wider problem of the causation of essential hypertension

**The intra renal circulation** Barclay, Trueta and their colleagues in experimental observations on rabbits have shown by means of radiographic studies and the injection of dyes that there are within the kidney two distinct pathways for the flow of blood

Blood entering the kidney and reaching the interlobular arteries may pass (a) by the cortical route to the glomeruli of the cortex and then to the cortical intertubular capillary network, or (b) by the medullary route which passes through the juxta medullary glomeruli and then to the vasa recta and direct to the interlobular veins

By means of a shunt mechanism the greater part or almost the whole of the blood entering the kidney may be diverted along the medullary route thus leaving the cortex ischaemic It appears that this shunt mechanism may come into operation whenever the total blood flow through the kidney is reduced, for example when the renal arteries are thrown into spasm by reflex nerve stimulation

These observations may be of significance in relation to essential hypertension and it is an interesting though yet unproved thesis that renin produced as a result of this shunt mechanism plays an important part in the causation of this disease On this theory, when the renal arteries are constricted as part of a generalized vasoconstriction brought about in the manner already discussed the shunt mechanism comes into play and induces ischaemia of the renal cortex which in turn gives rise to the production of renin and thus to persistence of the state of hypertension This vicious cycle can be broken by splanchnic section which abolishes the renal vaso-constriction relieves the cortical ischaemia and cuts down the production of renin

**The Course of Essential Hypertension** The progress of a case of essential hypertension can be divided into distinct phases In the early stages the elevation of blood pressure is probably not continuous but intermittent or at any rate variable and transient increases are brought about by excitement or mental stress or physical exertion Later the diastolic pressure becomes persistently elevated but at this stage it is

labile and can be reduced to the normal by sedation or by the administration of parasympathetic mimetic drugs such as tetra ethyl ammonium bromide. At this stage prolonged relief or even permanent cure can be achieved by splanchnic section.

If the hypertension is maintained for a longer period, organic changes appear in the blood vessels the characteristic feature being a fibrinoid necrosis of the walls of the arterioles. These changes can be demonstrated histologically after muscle biopsy, while their results are recognizable by examination of the eye grounds. Thus eventually the peripheral vaso spasm gives place to organic narrowing and the hypertension becomes irreversible. Life is usually cut short by cardiac failure or a cerebral vascular accident.

### TUMOURS OF BLOOD VESSELS, HÆMANGIOMA

A hæmangioma is the commonest tumour of childhood. It is often present at birth or becomes evident soon afterwards, and is rare in adult life except in the form of ruby spots in the skin of the abdomen and thorax (de Morgan's spots). It has been suggested they presage carcinoma—a view lacking corroboration.

Hæmangiomas are often multiple and vary in size from a tiny red or purple speck in the skin to a tumour which covers the whole face or a large part of a limb. The tumours most often involve the skin but may be entirely subcutaneous. Less commonly they are found in the liver, the lung, or in the mucous membranes of the mouth, larynx or alimentary tract. Rarely they arise in the bladder, the renal pelvis, and sometimes in the bones of the skull and the vertebrae. Angiomatous tissue is a common constituent of teratoid tumours.

The ætiology of hæmangioma has aroused considerable dispute. The various stages in blood vessel development provide abundant opportunity for the production of anomalies, so that probably all types are not alike in their origin, and many examples formerly classed as tumours are really developmental abnormalities. Those met with in childhood are of congenital origin and are believed to develop from angioblastic tissue that has not established its normal connexion with the circulatory channels. The blood corpuscles within the nævus must come from the general circulation, though the tumour does not have a close connexion with vessels of the adjacent tissues, it has its own supporting vessels (evidenced by injection experiment). Others, such as the "spider nævus" are probably in many instances due to localized dilatation of capillaries and therefore have a connexion with the vascular system. The familiar vascular telangiectasis seen on the legs or on the face is probably an exaggerated example of such a simple dilatation.

There are three chief histological types of hæmangioma (1) capillary, (2) compact and (3) cavernous. This classification, though arbitrary, is preferable to the older ones which grouped the tumours either according to the position they occupied relative to the skin (cutaneous, subcutaneous, and mixed), or according to their colour (capillary, arterial and venous).

A capillary hæmangioma may take any of several different forms



It is often present as a superficial blue or pink staining of the skin of the face—popularly known as a mother's mark or port wine stain. The affected area may be small, or it may involve almost the entire face, or part of a limb. In other instances and especially in babies, the tumour appears as a bright red swelling slightly raised above the surface of the skin. The tumour is usually small and circular and looks like a raspberry, or it may have a linear outline. When the tumours are multiple they may roughly conform to the distribution of one of the cutaneous nerves.

The "spider naevus" or *naevus araneus* appears as an aggregation of dilated and tortuous capillaries on the face or hands. This type is probably not a true tumour but merely a dilation of some of the cutaneous arterioles.



FIG. 111. Capillary hemangioma of skin. Note the endothelium-lined spaces containing scanty degenerate red blood corpuscles.

(Laboratory of Royal College of Physicians of Edinburgh.)

Microscopically, a capillary angioma is composed of a mesh work of endothelium lined, irregular channels of variable size containing a few degenerated red blood corpuscles. The endothelium is supported by a delicate reticulum of areolar tissue which contains fine blood vessels but the blood vessels do not normally communicate with the endothelial spaces of the tumour. The epidermis over the tumour is thin and delicate and may be pigmented.

**Hereditary Haemorrhagic Telangiectasis** This condition described fully by Osler is characterized by the development of multiple spider stellate or nodular telangiectases in the skin and mucous membranes. They are not present at birth, but appear usually after the age of twenty years. They affect any part but particularly the face, mouth and nose. Haemorrhage may occur from any site especially the nose. The disease is transmitted and exhibited by both sexes as a Mendelian dominant, and thus half the members of a family are affected. In a few instances cirrhosis of the liver may coexist, as may cavernous telangiectasis of the lung (see p. 346).

A compact hemangioma is believed to be derived from a capillary hemangioma whose cells have undergone massive proliferation. It is usually situated in the subcutaneous tissues and is solid or partly cystic. The skin is slightly raised and thinned over the tumour so that

it presents a bluish tinge. The tumour possesses a thin capsule, and on histological examination is found to consist of solid alveolar masses of round or cubical cells in which no trace of lumen is evident.

A cavernous hæmangioma consists of a number of blood spaces which intercommunicate. The spongy network of the tumour occupies not only the skin itself, but the subcutaneous or submucous tissues. A primitive type of endothelium lines the vascular channels. The tumour is usually present at birth and has a dark red or purple colour and irregular surface, it is often present about the head and face, especially the lips and buccal cavity. During the early months of life it may extend and infiltrate rapidly, and ulceration of its surface may lead to severe hæmorrhage.

A cavernous hæmangioma may arise primarily in bones, especially those of the skull, which may radiographically assume a honeycomb appearance.

Usually a hæmangioma is an innocent tumour, and it is characteristic of it that it tends to regress. This change is often observed at the first dentition, at puberty, or after an acute illness. But there are instances in which a hæmangioma has assumed malignant characters and has given rise to metastases in the lungs, with death from hæmorrhage or anæmia.

**Cavernous Hæmangioma of the Lung.** A hæmangioma of the lung may be single or multiple. When of the cavernous type it may result in an arterio venous fistula, the condition is rather a localized developmental structural defect of the blood vessels, especially the veins, than a true tumour. It is usually associated with hereditary hæmorrhagic telangiectasis.

In a typical example a considerable portion of a lobe of the lung is replaced by a sacculated venous network into part of which enters the greatly dilated and thin walled lobar artery. When inspected at operation the lobe shows expansile pulsation which persists on a reduced scale even after the lobar artery is ligated. The pulmonary vein draining the lobe is hugely dilated.

The arterio venous fistula is responsible for characteristic cardio-respiratory and other changes, the chief of which are cyanosis, dyspnea and polycythæmia. Death may occur from hæmorrhage.

**Malignant Hæmangioblastoma (hæmangio-endothelioma)** Sometimes a hæmangioma presents malignant features from the outset. Such a tumour may assume large proportions and metastasize by both the lymph and blood vessels. It has developed most often in the liver (which may be cirrhotic) the spleen, the lungs, and the retroperitoneal tissues.



FIG. 112. Cavernous Angioma of the lip.

**Arterial Angioma** *Cirsoid or Racemose Aneurysm.* This rare condition may arise in infancy or in adult life. It consists of an overgrowth of small arteries which are intertwined in racemose fashion. The arteries pulsate visibly giving an appearance likened by Virchow to a pulsating mass of earthworms. The veins and capillaries may be increased in number. Probably the condition is due not to tumour formation but a local developmental abnormality of the vessels.

In the great majority of cases a cirsoid aneurysm affects the side of the scalp and it tends to spread over the head and also to the upper part of the neck. The great vascularity of the growth induces decalcification of the skull and may eventually perforate it.

### VASCULAR OBLITERATIVE DISEASES

The blood vessels of the extremities may undergo gradual obliteration as a result of organic diseases such as arteriosclerosis, atheroma and thrombo-angitis obliterans. They may be occluded suddenly by embolism or thrombosis or they may undergo recurrent constriction in such vasospastic disorders as Raynaud's disease. The pathological foundation of these occlusions are of profound significance in the differentiation of the vascular disorders of the limbs.

The effects of circulatory arrest may be studied in patients suffering from arterial disease or more conveniently in normal subjects after the application of a tourniquet or an inflatable cuff to the limb. In the latter field particularly the work of Lewis and his colleagues stands pre-eminent.

**Discoloration of the Skin** When an inflatable cuff is applied and the pressure raised above the systolic blood pressure the first objective change is in the colour of the skin which first becomes deathly pale then congested and cyanotic and finally mottled.

The early pallor is due to draining of the blood from the skin capillaries into the more deeply placed veins as can be shown by microscopic examination of the nail beds.

The congestion and cyanosis appear within a few minutes and gradually deepen. They are due to regurgitation of the blood now deprived of its oxygen content, into the superficial capillaries which have undergone dilatation as a result of the direct action on their lining endothelium of vasodilator products of metabolism pent up in the adjoining tissue spaces.

The mottling of the skin is an interesting but unexplained phenomenon, which comes on gradually and is persistent. It consists of white areas, Bier's spots, with intervening zones of cyanosis and is to be regarded as due to local vascular constrictions of unknown origin.

**Temperature of the Limb** Clinical records often suggest that in a sudden vascular occlusion the limb rapidly becomes "stone-cold." It is obvious, however, that the loss of heat must be a gradual process and Lewis's observations indicate that a considerable time elapses before the limb reaches room temperature. Cooling takes place most rapidly in the distal part of the extremity and the tips of the fingers.

approximate to room temperature in about half an hour. The proximal part of the limb takes several hours to cool to this extent.

**Effect on Nerves** The nerves of the limb lose their function with some rapidity under ischæmic conditions. Within 15 minutes of a complete circulatory arrest there is numbness at the finger tips, and from this time on there is a gradual spread of sensory and motor paralysis up the limb. The paralysis is a temporary one however, and recovers within a few minutes after release of the tourniquet, though there may be some persistent weakness from direct pressure upon the nerves.

**Effect on Muscles** If the muscles of the ischæmic limb are contracted vigorously, severe pain is caused, owing, it is thought, to accumulation within the muscle of the products of activity which should normally be carried away in the venous blood. The pain is of cramp like character, a diffuse, continuous ache, felt in the muscles themselves, and very severe. It disappears rapidly after release of the tourniquet. This pain is similar in character to the pain of intermittent claudication seen in many cases of vascular obliteration, e.g., in arteriosclerosis. The pain comes on early in complete arterial obstruction, more slowly if the blockage is incomplete, and it thus forms a reliable index to the extent of the disease.

**Effect on Collateral Circulation** If the main artery to a limb is obstructed, the fate of the limb depends upon the extent to which the collateral circulation can be developed. The development of a collateral circulation is not so simple a process as might be imagined. The older view that the blood, denied entrance to the main artery, forced its way under an increased pressure along smaller channels, is no longer tenable. Indeed, the pressure proximal to the block is not increased but, on the contrary, lowered, with the result that the lumen of the artery between the block and the nearest collateral vessel proximally becomes reduced.

It seems likely that the immediate stimulus to the formation of a collateral circulation is the result of lowered pressure within the ischæmic territory. In addition the vessels within the ischæmic territory become dilated as a result of the accumulation of vasodilator metabolites from the tissues resulting in a diminished resistance to the blood flow along the collateral channels. The collateral vessels undergo dilatation and compensatory hypertrophy, and the blood flow to the extremity may finally be restored to its normal volume.

The extent of the collateral circulation, and the rapidity with which it can be opened, depend upon a number of factors, and especially upon the character of the obstructing agent and upon the condition of health of the collateral channels. If the obstructing agent is a simple ligature, the minimum amount of clotting occurs in the vessel proximal and distal to it, and all available collaterals can be utilized. On the other hand, if the obstruction is caused by thrombosis in an arteriosclerotic artery, or even by an embolus, it is sometimes found that several collateral channels are obstructed owing to spread of thrombosis within the main artery. The condition of the collateral channels has an obvious importance, if healthy, they undergo considerable dilatation under the influence of the vasodilator products, whereas if diseased they may

be quite incapable of dilatation. The estimation of these potentialities is of outstanding importance in the treatment of disorders of the circulation.

**Tests of Vascular Obliteration** In severe cases the presence of vascular impairment is obvious. The limb is generally colder than its fellow, pale or cyanotic, the pulse is diminished or absent, the vessels may be palpably thickened, signs of gangrene may be evident.

For less marked cases, and in order to estimate the degree of impairment, the following tests may be carried out —

(1) *Pulsation of Peripheral Vessels* In the lower limbs pulsation may normally be felt in the femoral artery at and below the groin, in the popliteal artery, in the posterior tibial artery behind the medial malleolus and in the dorsalis pedis artery at the ankle. In vascular disease pulsation is lost in the reverse order. Absence of pulsation does not necessarily signify that the vessel is obliterated, there may be a continuous flow of blood, non-pulsatile due to blocking of the main vessel proximally. In borderline cases pulsation may return if the peripheral vessels are dilated by warmth, this may be effected by warming the limb, or, better, by applying heat to the trunk so as to warm the arterial blood going to the limb, pulsation may also return during pyrexia.

To test for the presence of pulsation in a doubtful case an oscillogram may be used. This is a cuff applied to the part to be tested, inflated and connected with an aneroid manometer or a special instrument. Oscillations similar to those observed during blood pressure estimations are demonstrated, and may be recorded graphically.

(2) *Skin Temperature Tests* The skin of the affected limb should be compared with its fellow (a) as the two limbs lie in bed, (b) after exposure for a few minutes to the cold air, (c) after immersion for a few minutes in water at body temperature. The skin temperature may be gauged with fair accuracy by touch, preferably using the back of the fingers or special skin thermometers or thermo-electric couples may be used for exact records. In a limb of impaired vascularity the temperature is normal when the limb is protected by bedclothes, but cools more rapidly on exposure and warms less readily when heated.

(3) *Elevation of the Limb* If the two limbs, thoroughly warmed to eliminate spasmodic vasoconstriction, are raised above the level of the body, say to 45 degrees, the limb with diminished vascularity becomes deathly pale. For purposes of comparison, the level at which this sign develops may be recorded.

(4) *Tests of Vasodilatation* Normally all the vessels of a limb are in a state of tonic vasoconstriction. When the main vessels are obliterated by disease, the nutrition of the extremity depends upon the degree to which the collateral vessels can dilate. If the collateral vessels are healthy, improvement may be effected if the vasomotor control can be abolished by paralyzing the sympathetic innervation, if, on the other hand, they are diseased, little or no improvement can be expected.

To assess the benefit to be expected from sympathetic denervation the vasomotor control may be abolished temporarily in the upper limb by anesthetizing the cervico-dorsal sympathetic trunk with novocain,

or in the lower limb by inducing spinal anesthesia. The skin temperature of the extremity is estimated accurately before, and at intervals afterwards, and the response noted. If the collateral vessels are capable of dilatation, the skin temperature rises abruptly, perhaps to within a few degrees of blood temperature, if they are diseased, the rise is slower and incomplete.

In a typical case, at room temperature  $15^{\circ}\text{C}$ , the skin temperature of the extremity may be about  $18^{\circ}\text{C}$ . If the collateral circulation is healthy, after induction of the anesthesia the temperature may rise to  $30^{\circ}$  to  $31^{\circ}\text{C}$ , if diseased to  $25^{\circ}\text{C}$  or so.

Another method, applicable to either upper or lower limbs is to abolish vasomotor control by raising the temperature of the blood going to the limb. This may be effected by heating the trunk in a heat cage, or by immersing one of the limbs not being tested in hot water.

### ARTERIAL DEGENERATIONS

The nature, incidence and supposed causes of the various forms of arterial degeneration are inadequately treated in most text books of medicine and of general pathology, and here it will only be necessary to describe those aspects of surgical interest.

It may be recalled that the various degenerations are of common occurrence in the male sex after the age of fifty or sixty years, and that when they occur at an earlier age they are generally associated with some specific cause such as syphilis, diabetes, nephritis, alcoholism or plumbism. Further more, it may be mentioned that at least three fairly distinct types of degeneration are recognized: (1) *Atheroma*, a patchy disease principally affecting the aorta, the coronary and cerebral vessels, and characterized by fatty and fibrous changes in the deeper parts of the intima, with loss of elasticity and finally softening and the formation of "ulcerated" plaques. (2) *Arteriosclerosis*, a widespread affection characterized by more or less generalized increase of the fibrous tissue elements of the arterial wall. (3) *Annular calcification* (Mönckeberg's sclerosis), characterized by fibrosis and calcification of the middle coat of medium sized and smaller vessels.

The various forms of arterial degeneration are of especial interest for the surgeon, for by narrowing the peripheral vessels and interfering with their elasticity these diseases cause progressive impairment of the blood supply, and ultimately may lead to gangrene. In subjects otherwise healthy the

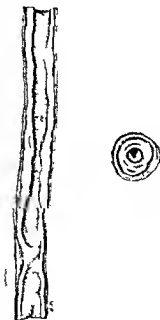


FIG 113 Diabetic end arteritis of the femoral artery  
(By courtesy of Prof J W S Blacklock)

circulation may become much diminished, yet suffice to maintain the vitality of the part, and consequently gangrene rarely supervenes before the age of sixty five or seventy years (senile gangrene). In subjects affected by diabetes, on the other hand, the presence of the poisonous products of faulty metabolism greatly reduces the vitality of the tissues and lessens their resistance to infection, and consequently gangrene occurs at a somewhat earlier age (diabetic gangrene).

**Senile Gangrene.** This condition affects males far more frequently than females, and it is uncommon before the age of sixty-five years. The gangrene is generally preceded by premonitory indications of the failing vascularity of the part, such as numbness, tingling, cold, and severe cramp-like pains. The great toe is most commonly the part first affected, especially on the dorsum, close to the nail. Often the onset of the gangrene is determined by slight trauma or by mild infection, such as may follow the removal of a corn.

The skin of the toe at first is dead white; later it becomes discoloured by altered blood pigment, and, finally, it becomes black, shrunk and mummified. Since the reduction of vascularity occurs slowly, there is no flooding of the part with venous blood and no sudden stagnation of fluid in the tissues. Consequently the part usually remains dry—at least, near the skin surface—and little, if at all, infected.

The disease progresses very slowly and, indeed, may remain with little change for a period of months. Later the other toes may be involved, and eventually the remainder of the foot. At any time the access of infection may lead to great increase in the rapidity of spread. If the blood supply to the zone bordering on the gangrenous part be adequate an inflammatory reaction may occur, and ultimately result in a line of demarcation. After a very long period the gangrenous part may be shed, and since the blood supply to the muscles and bones is more liberal than to the skin, the resulting stump is conical.

**Diabetic Gangrene.** This condition is more properly termed “arteriosclerotic gangrene occurring in diabetic subjects,” for it is due primarily to sclerotic changes in the vessels, though the progress is accelerated and aggravated by the underlying disease.

Diabetic gangrene is commonest in male subjects, and it is rare before the age of fifty years. Like senile gangrene, it begins almost invariably in the foot, especially in the neighbourhood of one of the toe-nails. The toxic products of faulty fat metabolism, which are responsible for many of the general effects of diabetes, precipitate its onset even before the arteriosclerotic change is far advanced. Moreover, the toxic products impair the resistance of the tissues to infection and diminish the general vitality of the patient, so that rapid extension to the foot complicated by infection is usual.

**Embolic Gangrene.** This form of gangrene is not common, but it is of particular importance because a timely removal of the obstructing embolus from the affected vessel may restore the circulation. Migrating emboli usually take the form of a partly organized clot which has developed usually in the left auricle as a result of circulatory stasis in the course of a decompensated heart lesion; less often it arises from the surfaces of an atheromatous ulcer in the aorta. It has occurred as

a rare post operative complication in stout subjects. It is the large arterial trunks, such as the bifurcation of the aorta, the iliac, the femoral and brachial arteries, which entrap the embolus. The femoral artery is by far the commonest site (54%). The embolus is arrested where an artery narrows, its point of bifurcation, and usually it straddles it. Arrest of the circulation leads at once to severe pain from ischaemia, pallor followed by lividity, and, after a variable interval, gangrene at a level depending on the site of vascular occlusion. The advent of gangrene is the outcome not of the local vascular obstruction but of vascular spasm and progressive intravascular clotting extending distally from the embolus.

### RAYNAUD'S AND ALLIED DISEASES

In 1862 Maurice Raynaud described a number of cases of obscure aetiology, in which the most prominent features were intermittent pallor and cyanosis of the extremities precipitated by cold. It is now recognized that this syndrome, generally described as the *Raynaud phenomenon* is not attributable to a single disease, but may occur under the following conditions —

(1) In healthy persons subjected to extreme cold long enough to lower the body temperature by several degrees.

(2) In sufferers from so called *hereditary cold fingers* a familial disease affecting either sex and generally originating in childhood.

(3) In workers using vibrating tools e.g., pneumatic drills and riveters.

(4) In the incipient stages of degenerative vascular diseases, such as thromboangitis obliterans, arteriosclerosis etc. and of sclerodactyly.

(5) Idiopathically.

The term *Raynaud's disease* is best restricted to the idiopathic form. This is a rare affection, which occurs almost exclusively in women appearing first between the ages of twenty and forty years. It affects the fingers and hands and sometimes, though usually less severely, the feet as well, the nose and ears are not affected. The attacks, which are nearly always symmetrical are precipitated by exposure to cold (say, 18° C), but in about half the cases emotional disturbance may be responsible. The colour change in the skin is a dusky blueness starting in the finger tips and associated with numbness and pain, followed usually by a waxy pallor if the stimulus persists. Warming of the part terminates the attack and the skin assumes a lobster red colour, which gradually fades. No bleeding follows a prick of the finger during an attack. Between attacks the skin is usually normal. Without treatment the condition may progress and culminate in superficial ulcerations or even in rare instances gangrene of the skin, especially of the little and ring fingers.

The aetiological factors are not yet understood. That emotional disturbance may precipitate attacks suggests that an endocrine or centrally originating vasomotor influence may be responsible for the peripheral vaso constriction, but against this supposition is the observation that



regional "nerve block" will not abort an attack in progress and that sympathetic denervation does not entirely abolish their repetition. Lewis's detailed studies afford strong evidence that the colour changes are due to obstruction in medium-sized arteries, due to an unexplained fault in their vasomotor tone—an unusual susceptibility of the vessel walls to cold. Only in the advanced stages is there any obliteration of the smaller vessels.

*Acrocyanosis* resembles Raynaud's disease except that the blanching phenomena are absent. During the attacks, which follow exposure to cold, there is usually diminished sensibility or even anaesthesia within the affected area of skin. Pain is absent during the attack, but it may be severe and burning in character as it passes. The hand assumes a vermilion red colour at the termination of an attack. Trophic ulceration of the skin may occur in progressive cases.

*Erythrocyanosis frigida* (known also as Bazin's disease) affects young women whose legs are unusually fat and thick. In winter the skin of the lower part of the backs of the calves and the ankle region becomes the seat of dusky reddish purple indurated patches. The malady is bilateral, worse usually on one side than the other, and in severe cases the skin over the discoloured patches breaks down, leaving indolent shallow ulcers.

Part of the swelling of the legs is due to overgrowth of subcutaneous fat and areolar tissue. It may be particularly excessive in the form of pads about the lateral malleolus. The presence of giant-cell formations in the tissue removed from the leg ulcers led to the supposition that tuberculosis might be an underlying cause. More likely the giant cells are of the foreign body type associated with the necrotic process.

### THROMBO-ANGELITIS OBLITERANS

This disease was first described, under the title *endarteritis obliterans*, by v. Winiwarter in 1879, but it has only received widespread recognition since Buerger in 1908 drew attention to its characteristic features and gave it the name it now bears.

Thrombo-anginitis obliterans is a disease of arteries and veins. In the majority of cases it affects the vessels of the lower limb but sometimes it involves those of the forearm, and, exceptionally, the testicular and other vessels. It is characterized by low-grade inflammatory changes in the vessel walls with thrombosis in the lumen and much fibrosis in the perivascular tissues, and it takes a progressive course which may culminate in gangrene of the affected extremity. The vessels of the opposite limb may be involved subsequently, sometimes after the lapse of several years.

Unlike most other forms of vascular disease, thrombo-anginitis obliterans begins before the age of fifty years, and frequently it occurs between the ages of twenty and forty years. It is almost certainly limited to males.

The cause of the disease is unknown. There is no demonstrable relation to syphilis, tuberculosis, arteriosclerosis, or other disease.

The pathological changes are those of a low grade inflammatory process, and it has been presumed that the cause is some form of infection or toxæmia. The valuable therapeutic result achieved in early cases by sympathectomy suggests that arteriospasm of nervous origin may be a factor in its causation. It is well recognized that such spasm if long continued may lead to marked organic changes in the vessel wall.

In the affected region the most striking pathological change is perivascular fibrosis, and this may be so extensive as to bind the artery with its vein and any accompanying nerves in a dense cord of cicatricial tissue, from which they can only be dissected with difficulty. The

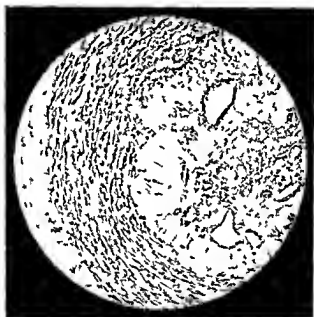


FIG. 114. Thrombo arteritis obliterans. The lumen of the artery is occupied by organized thrombus which has been recanalized.

(Department of Pathology University of Glasgow.)

artery when cut across is seen to be contracted, the wall greatly thickened, and the lumen narrowed or quite obliterated.

Microscopically, there is an infiltration of all the coats of the vessels by lymphocytes and plasma cells. The intima is somewhat thickened by proliferation of its endothelial cells, and the muscle fibres of the media are atrophied, but the greatest change is seen in the adventitia, which is extensively infiltrated by fibrous tissue. The internal elastic lamina is not destroyed as in atheroma, but is thickened and sometimes duplicated.

The lumen of the vessel is occupied in whole or in part by a thrombus, which in old standing cases is organized and fibrous. Sometimes the thrombus contains accumulations of round cells with occasional giant cells of the foreign body type. Canalization of the thrombus occurs as in other forms of intravascular clotting. The new channel may

be visible as an irregular, centrally placed lumen, but it is never of large size, and since the fibrosis around prevents dilatation it does not suffice to maintain the nutrition of the part.

Thrombo-angiitis obliterans is a slowly progressive disease. Usually it appears first in the main vessels of the foot and leg especially in the dorsalis pedis artery and in the distal portions of the anterior and posterior tibial arteries. Later it tends to spread proximally and may involve the popliteal artery and even the femoral and iliac vessels. The distribution of the disease is not uniform but patchy, and a vessel diseased over a length of a few centimetres may be unaffected in the rest of its course.

Since the disease is at first confined principally to the larger blood vessels and is of slow progress, a collateral circulation usually develops sufficiently to maintain, though imperfectly, the nutrition of the limb, but eventually as the obliterative process extends and especially when the popliteal artery is occluded, the collateral circulation proves inadequate and gangrene results. The gangrene is usually of the dry type, and remains confined for long to one or more of the toes.

Gangrene, although the final result, is by no means the most distressing one. For a long time before this stage is reached, impoverishment of the blood supply and involvement of nerves in the perivascular fibrosis give rise to recurrent or continuous pain. Ischaemia of the muscles causes paroxysmal cramp-like pains after even gentle exercise. Impaired nutrition of the tissues, and involvement of autonomic nerves, lead to coldness, blueness or oedema of the extremity and to painful superficial ulcers about the toenails. Phlebitis of superficial veins adds to the discomfort. Eventually pain may be so great as in itself to justify amputation.

## VARICOSE VEINS

Dilated and varicose veins occur most frequently in the lower limbs, in the anal canal (haemorrhoids), and in the spermatic cord (varicocele) but in various conditions of disease they may occur in many other parts of the body. In the situations mentioned the varicosities depend upon several related factors, which will be considered in more detail below. In other situations varicosity is almost invariably the result of obstruction to the normal venous flow—for example, the varicosities at the lower end of the oesophagus and elsewhere in cirrhosis of the liver, those of the superficial abdominal veins in thrombosis of the inferior vena cava, and those of the superficial thoracic and cervical veins in obstruction of the superior vena cava. One exception to this general statement is the varicosity which follows establishment of an arterio-venous aneurysm, in which the dilatation of the vein is due to the intensified pressure from the inflow of arterial blood (see p. 226).

### Varicose Veins in the Lower Limb

Varicose veins in the lower limb affect adults at any age, and they are especially common between the ages of twenty and forty years.

The varicosity may affect any of the superficial veins of the lower limb and not uncommonly the condition is bilateral. The main trunk and principal tributaries of the great saphenous are the veins most frequently affected. Sometimes only a short segment of a single vein is noticeably dilated, but more often the dilatation is widespread and may affect every subcutaneous vein in the limb to a greater or less extent. In some subjects, especially stout elderly females, innumerable cutaneous venules participate in the dilatation.

From the ætiological standpoint two distinct types of varicose veins may be recognized. Of these the second type is the commoner and the more important.

(1) In the first type the cause is some organic obstruction to the venous return flow, such as may result from the pressure of an intra-abdominal tumour or fluid collection or from extensive thrombosis in the main venous trunks. Post-operative thrombosis (phlegmasia alba dolens) and thrombophlebitis complicating such infections as pneumonia and typhoid fever, are examples of such organic obstruction, and they notoriously give rise to very extreme forms of varicosity. It seems probable that the varicosities that occur so often during pregnancy belong to this class and result from pressure of the enlarged uterus on the pelvic veins. The special practical importance of this type lies in the necessity for recognizing the futility of local treatment unless, or until, the primary cause be overcome.

(2) In the second, the more common type, no organic obstruction is present. This is the form so common in young adults. It affects males more often than females and a familial incidence may be discernible. From the ætiological standpoint this type is of especial interest, for it is apt to occur in two totally distinct classes of subject, namely, in hyposthenic subjects of sedentary occupation, and in athletes.

The cause of varicose veins of this type is generally assumed to be related to some congenital weakness in the vessel wall or supporting tissues, which may be accompanied by, or lead to, a deficiency of the valves. The valvular incompetence thus produced subjects the veins to an increased pressure from within, and, in the upright position, to the weight of an extended column of blood reaching as far as the heart. In addition to such hypothetical developmental weakness, however, there are probably other causative factors, which are related to the general structure and efficiency of the venous system.

In this connexion Wood Jones has drawn attention to several features in the anatomy of the venous pathway which deserve more general recognition. Venous blood, unlike arterial blood, has no *vis a tergo* from the heart beat, nor have the veins more than slight intrinsic pulsatile contractibility, and consequently, in the lower limbs, where gravity increases the difficulty of the venous return, the blood flow depends principally upon the contractions of the skeletal muscles.

Now, in so far as the deeply situated veins are concerned the anatomical disposition is such as to assist this propelling action on the part of the muscles. The deep veins of the leg form multiple channels, irregular and variable *venæ comites*, buried deep in the muscle masses

and necessarily compressed by every muscular contraction. At the flexure of the joint these several channels converge upon a single large vessel, the popliteal vein, and this vein is furnished with two or three bicuspid valves, which effectually prevent regurgitation of blood when the muscles relax. A somewhat similar disposition obtains in the thigh.

The superficial veins, on the other hand, lie unsupported in loose subcutaneous tissue, and in normal circumstances are merely subsidiary. Between the superficial and deep systems, however, are several communicating channels, notably at the saphenous opening and at the popliteal space, and in conditions in which the pressure in the deep veins is raised these communicating channels transmit the excess blood to the superficial system, which thus becomes a temporary receptacle for the excess blood.

In sedentary persons gravitation effects a passive venous congestion of the whole limb. The deep veins being surrounded by muscles are well supported, and transmit the increased pressure to the superficial veins, and these, being unsupported, dilate. In athletes, on the other hand, there is an active venous congestion, following the increased vascularity of the contracting muscles. Moreover, in athletes the muscle contractions, being sustained rather than intermittent, have no pump-like action, but, on the contrary, tend to obstruct the deeply placed veins, and thus the blood is diverted superficially.

The effects of varicose veins (of whatever cause) are characteristic. The veins dilate, increase in length and become tortuous and often sacculated. The vessel wall becomes thickened by fibrosis and its muscle fibres atrophy, with the result that the vessel when cut or ruptured gapes widely, permitting free and sometimes fatal hæmorrhage. Adjacent portions of a tortuous vein may become bound together by fibrous tissue and are often closely adherent to the skin, which itself ultimately undergoes atrophic changes.

Stasis of blood in the veins and congestion in the perivascular tissues lead to the deposition of hæmosiderin, and when the veins lie close to the surface, as on the medial surface of the leg, the skin may become deeply pigmented.

Irritation by the pigment, combined with diminished vitality of the tissues from congestion, and often assisted by the effects of dirt and infection, may lead to dermatitis in this region, and later to the formation of an ulcer, which is slow to heal and very apt to recur.

In addition, varicose veins are very liable to thrombosis and phlebitis, which may follow injury or may arise in the absence of any demonstrable cause. Thrombosis may subsequently lead to the formation of small calcified nodules (phleboliths) in the obliterating thrombus.

### Hæmorrhoids

Internal hæmorrhoids result from dilatation and varicosity of the superficial veins of the anal canal. These vessels, which are anastomosing channels between tributaries of the superior and inferior hæmorrhoidal veins, lie in the submucous tissue superficial to the sphincter muscles, and being ill supported they readily dilate.

In the great majority of cases the essential factor in the production of hæmorrhoids is chronic constipation. The presence of large scybalous masses in the rectum induces a degree of venous stasis, and this is greatly aggravated by prolonged straining at stool. It seems probable that in some subjects there is a weakness of the vessel walls, which predisposes to the dilatation. Occasionally hæmorrhoids arise as a result of obstruction to the portal blood flow, for example, in cirrhosis of the liver. Hæmorrhoids are of common occurrence in pregnancy, from pressure of the enlarging uterus upon the superior hæmorrhoidal vein. It is important to recognize also that they may result from the pressure of a tumour within the rectum, and may provide the first indication of such disease.

Fully developed hæmorrhoids form dark purplish polypoidal masses which project into the anal canal. Most commonly three large hæmorrhoidal masses are present, one situated anteriorly and the other two on the posterolateral aspects of the canal, and in addition there are usually several smaller masses. The masses tend to protrude at the anus, usually only during prolonged straining at stool, but sometimes upon the slightest exertion. Even when small they may bleed freely and may even give rise to a severe degree of secondary anæmia. Infection may occur, especially if the masses remain protruded at the anus. Infection commonly leads to thrombosis within the hæmorrhoidal vein and sometimes to ulceration or necrosis of the pile. Rarely such infection has been known to lead to pyelophlebitis.

External hæmorrhoids result from dilatation and varicosity of anastomosing veins situated deep to the perianal skin. Commonly they give rise to small firm piles or skin tags. Occasionally the vein ruptures as a result of sudden straining at stool and the extravasated blood clots, forming an exceedingly painful "thrombosed pile."

### Varicocele

This is a varicose condition of the veins of the pampiniform plexus. It occurs in young men and is almost always confined to the left side. Little is known of the etiology, but it seems probable that, as in varicose veins of the lower limbs, there is a developmental weakness of the vessel walls. The affected veins become dilated and extremely tortuous and from the weight of the contained blood they may cause discomfort.

Varicocele may occur in older men and is then usually due to pressure of a tumour upon the testicular vein or, on the left side, on the renal veins. A hypernephroma of the left kidney growing along the lumen of the left renal veins has been known to have this effect.

### TRAUMATIC ASPHYXIA—Traumatic Cyanosis

This rather rare condition results from severe but briefly sustained, crushing injuries to the thorax, such as may occur in railway or pit accidents or rarely, from the pressure in densely packed crowds. It is characterized by a generalized purple suffusion and œdema of the skin of the face and neck and diffuse ecchymosis of the conjunctiva. It may be accompanied by fracture of the sternum or ribs, and from

injury to the minute vessels in the retina it may lead to temporary or permanent blindness

The distribution of the very striking discoloration is sharply demarcated. In front it extends to a short distance below the clavicles posteriorly its inferior limit is variable but it usually reaches the level of the upper part of the shoulder girdle.

The condition is due to sudden distension of the veins of the upper part of the head and neck as a result of sudden occlusion of the large veins at the thoracic inlet and the peculiar character and the wide extent of the lesions are attributed to the absence of valves in the cervical veins.

The discoloration of the skin is due to dilatation of veins and capillaries associated probably with temporary loss of their elasticity. Hemorrhage of any considerable size is very unusual. The œdema and suffusion recede gradually and with less change of colour than is observed when an ecchymosis fades. Before absorption is complete the skin may have a blotchy yellow green colour which is slow to disappear.

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## CHAPTER XII

### DISEASES OF LYMPH GLANDS AND VESSELS

By reason of their intimate relationship to the tissue spaces the lymph channels form an easy route for the spread of bacterial infections and for invasion by malignant cells. Consequently the lymph vascular system is of primary importance to the surgeon in relation to acute and chronic infections and to malignant neoplasms.

The radicles of the lymph system originate in minute intercellular culs de-sac, and by union they form larger vessels which terminate in the lymph glands. Efferent vessels from the glands eventually empty their contents into the venous blood stream, either by the thoracic duct or by other main lymph channels. A typical lymph gland is somewhat kidney shaped, and it consists of a fibrous capsule, from whose deep surface spring fibrous trabeculae, and a parenchyma of lymphoid tissue. A more or less distinct hilum may be recognized, which admits the artery to the gland and forms the point of exit for the veins and the efferent lymph vessel.

The afferent lymph vessels, usually multiple, enter the gland at its convex surface, and, having pierced the capsule, they communicate directly with a subcapsular lymph space known as the "corridor" of the gland. Lymph percolates through the meshes of the corridor and thence to finer channels known as lymph sinuses. In the sinuses the lymph stagnates in close contact with the endothelial cells of the lymph cords, and any particles such as bacteria or pus cells may be arrested there and undergo phagocytosis. From the sinuses the lymph passes towards the hilum of the gland and is collected into the main efferent vessel.

It may be noted that a lymph gland subserves two distinct functions, the one concerned with arrest and destruction of substances in the lymph, the other with the formation of lymphocytes by the germ centres of the follicles. Each of these functions is of great importance in relation to the pathology of the lymph vascular system.

### OBSTRUCTION OF LYMPH VESSELS

Obstruction or obliteration of lymph vessels is a common result of acute and chronic inflammatory diseases and of cancer. When the obstruction is localized the collateral channels are usually sufficient to carry on drainage, but when the obstruction is extensive or involves large lymphatic trunks stagnation of lymph in the tissues results, and the affected part becomes oedematous, or, in the case of serous cavities, an effusion occurs. In many cases lymphatic obstruction is temporary and its effects disappear when the disease responsible for it subsides, but in other cases, especially those associated with cancer or chronic



infective disease, the obliteration of the lymph vessels is progressive and permanent, and a state of chronic oedema is established. Lymphatic obstruction is encountered most often in the lower extremities, the external organs of generation, and less often in the upper extremity. The obstruction may be due to extensive removal of lymph glands, to infective diseases, such as erysipelas or tuberculosis, or to widespread invasion of the lymph glands and their tributaries by cancer cells. In some instances a combination of factors is present.

The lymph vessels and the veins are functionally very similar, and their intimate association is evidenced by the great increase in lymph flow which occurs in a limb when its main vein is ligated. In the same way, probably, the veins may, in part, compensate for the effects of obstruction of the lymph vessels. In many diseases lymphatic and venous obstruction coexist, and when the obstruction is severe a very marked state of temporary or permanent oedema occurs which may finally give rise to the condition known as *solid oedema*.

**Elephantiasis.** Elephantiasis is a condition of overgrowth of the skin and subcutaneous tissues in a part subjected to prolonged lymph vascular obstruction. It occurs most often in the lower extremities and the external genital organs, and less often in the upper extremities and in the face. The swelling is due essentially to obstruction of the lymph vessels and glands in various ways, but as it is often preceded by a condition of solid oedema it is generally held that there must also be obstruction of the venous return in the affected part. The obstruction of the veins is usually due to thrombophlebitis caused by secondary infection from the skin or the blood.

The oedematous fluid in which the tissues are bathed is rich in protein and stimulates proliferation of fibrous tissue beneath the skin. On account of the stress from within and stagnation of lymph, the skin becomes coarse, thick, and corrugated, and is often discoloured. Sometimes it bears wart like projections, or it may exhibit excoriation or ulceration. It is noteworthy, and of great importance in relation to treatment, that the oedema is limited to the skin and subcutaneous tissue. By contrast the muscles are entirely normal.

Various types of elephantiasis are described according to the diseases which originally determined the lymph vascular obstruction.

*Congenital elephantiasis* is a rare affection of unknown causation. It is sometimes familial. One lower extremity is usually involved. The swelling is not very great in early life, but it increases during adolescence, and if untreated it eventually becomes enormous.

*Filarial elephantiasis* is the commonest variety and occurs in tropical countries. It is due to invasion of the lymph vessels and glands by the adult worm of the *filaria sanguinis hominis*. It is believed that the filarial infection is merely a predisposing cause of the lymph-vascular obstruction, and that the exciting cause is lymphangitis, due to superadded septic infection from foci elsewhere.

The disease attacks any part, but the lower extremities and the external genitals are the common sites, and the enormous size which these parts may assume is well known. When incised at operation the skin and subcutaneous tissue are found to be irregularly thickened, due

to overgrowth of the fibrous tissue and to the loculation of ordumatous fluid. The superficial veins are often dilated.

*Lupus elephantiasis* now rare occurs in young women and usually follows upon lupus of the toes and feet which has extended to the subcutaneous lymph vessels. As the lymph vessels become obliterated the skin and cellular tissues become hypertrophied. The skin is studded with fungating masses or ulcers of a livid blue colour. There is usually a concomitant infection by pyogenic organisms which may lead to gangrene.

*Elephantiasis graecorum* is due to infection of the skin and subcutaneous tissues with the lepra bacillus. The disease chiefly attacks the face, which becomes the seat of tumour like masses consisting of leprous nodules.

*Elephantiasis due to cancer* is seen in its most characteristic form in the upper extremity as a result of obstruction of the axillary lymph glands and the axillary vein in carcinoma of the breast. Sometimes it follows operation. The whole limb is enormously swollen and may be the site of multiple ulcers. Usually there is considerable pain, or the limb may be rendered useless.

*Elephantiasis neuromatosa* is a condition sometimes associated with neurofibromatosis. It is described on p. 319.

### ACUTE LYMPHADENITIS

Acute inflammatory enlargement of a lymph gland may result from any infective process in its catchment area. It is especially apt to follow interstitial infections with pyogenic organisms, particularly streptococci, and is less common in catarrhal conditions. The lymph glands affected most frequently are those of the antecubital fossa and the axilla in infections of the hands, those of the neck in infections of the scalp, face, tonsil or pharynx, and those of the inguinal region in infections of the genitalia and the anal region.

The earliest result of infection of a gland is proliferation of the endothelial cells lining the lymph sinuses, and these cells by their phagocytic action are able to deal with many of the organisms as well as the effete pus cells borne in the lymph from the initial focus. If the infection is more severe, the lymphoid tissue plays merely a passive part, and an inflammatory reaction similar to that seen in other tissues occurs. The blood stream is slowed, fibrinous fluid exudes and polymorph leucocytes escape into the meshes of the gland. At this time the gland is enlarged, congested and very tender. If the infection is overcome, the inflammation may resolve completely, but if the infection continues suppuration results. The abscess thus formed may remain limited to the gland, and may subsequently undergo partial absorption, fibrosis and calcification, but much more often it spreads beyond the confines of the gland, extends widely in the tissue spaces and gives rise to serious local and constitutional effects.

### CHRONIC NON-SPECIFIC LYMPHADENITIS

Chronic non specific lymphadenitis is a comparatively uncommon condition for the reaction of lymph glands to infection is so vigorous

that any inflammation short of suppuration subsides as soon as the primary focus of infection is overcome. Consequently chronic lymphadenitis is due almost invariably to the persistence of the primary focus of infection. Such chronic primary foci occur most commonly in the gums, the teeth, the tonsils and the scalp and consequently the glands the seat of chronic lymphadenitis are those of the neck.

### TUBERCULOSIS OF LYMPH GLANDS

The important part played by the lymph vascular system in the early spread of tuberculosis has already been discussed (Chapter IV), and it only remains to consider the special pathological features of the disease in lymph glands.

Tubercle bacilli usually gain entrance to the body in the pharynx,

the lungs, or the small intestine, and consequently the glands first affected are generally those of the neck, the lung hilum, or mesentery. Tuberculosis of lymph glands usually pursues a chronic course, and often remains limited during a long period to a single gland or a group of glands.

Other glands may be infected by way of the lymph or, rarely, by the blood stream, and the localization and character of the lesions differ according to the method of spread. Lymph borne infection progresses slowly and at first attacks the glands that are close to the primary focus, whereas a blood borne infection is just as apt to attack distant as local glands. On account of the anatomical distribution of the afferent lymph vessels



FIG. 113. Tuberculosis of lymph glands. Numerous lymph glands occupied by caseous material are matted together in a solid mass.

(Department of Clinical Surgery, University of Edinburgh.)

the early lesions in lymph borne infection are situated in the sub-capsular region of the gland in close relation to the subcapsular lymph sinus, whereas in blood borne infection since the blood vessel to a gland breaks up immediately on entering the hilum, the early lesions are scattered diffusely through the gland.

The pathological changes in a tuberculous gland may take either of two forms (a) the caseating, or (b) the proliferative. Of these the former is by far the more common.

(a) In the caseating form the changes are those typical of tuberculosis in most other situations. Tuberculous follicles develop, with a

central area of endotheloid cells and giant cells and a surrounding zone of lymphocytes. Caseation occurs in the central area, and enlargement of the caseous region and confluence of adjacent tubercles may proceed until the whole gland is replaced by yellow cheesy material. At any stage in the process the disease may be overcome, and then the follicles become replaced by fibrous tissue and ultimately become calcified. Such calcified tuberculous glands are extremely common, especially in the mediastinum or the mesentery of the small intestine, and less often in the neck.

If, on the other hand, the disease progresses, the periglandular connective tissues are involved, and adjacent glands become adherent to one another. Cold abscesses may develop and may infiltrate fascial planes and muscles. Eventually they reach the skin surface and rupture, leaving a tortuous sinus which remains as long as the glandular infection persists.

(b) In the proliferative form the pathological changes are of a different type. Giant cell systems are scanty or absent, and there is little or no caseation. The glands are swollen and elastic to the touch, and on section they are of fleshy appearance and greyish pink colour. Microscopically, the characteristic change is a diffuse proliferation of endothelial cells, with a variable degree of fibrosis. It will be obvious that glands affected in this way bear a certain resemblance to the glands of lymphadenoma (*see p. 256*), and not infrequently distinction is difficult.

**Tuberculosis of Glands in the Neck.** This condition presents certain characteristic features, and in view of its surgical importance merits separate consideration.

Two distinct types of infection may be recognized. In the first, the adenitis is a manifestation of widespread tuberculosis. The patient is thin, pale and anæmic, and active disease is present in the tracheo-bronchial lymph glands, and often in the lungs. The affected cervical glands are multiple and are situated in both sides of the neck mainly in the lower parts of the anterior and posterior triangles. The glands are not greatly enlarged, and are of soft consistency, rarely caseous.

The second type, seen more often in surgical practice, is a purely local infection. The patient, usually a child, is often of healthy appearance, and without evidence of other tuberculous lesions. Generally, one gland is grossly diseased, whilst a few glands adjacent to it are involved to a smaller extent. In most cases the principally affected gland is the jugulo-digastric or tonsillar gland, situated in the angle between the common facial and internal jugular veins. Less often a gland in the submaxillary region, or in the posterior triangle or the lower part of the neck, is the chief site of the disease.

It seems probable that in this local type of disease the infection gains access to the gland directly from the pharynx, and in the majority of cases the site of entry is at the tonsil. The infecting organism is often of bovine type, and in many cases, no doubt, is milk-borne. Frequently a predisposing factor may be found in a recent attack of acute tonsillitis or one of the infectious fevers of childhood, particularly measles, whooping cough or scarlet fever.

In this local type of disease the gland principally involved often progresses to caseation and to the formation of a cold abscess. From the tonsillar gland the abscess tracks forwards and downwards to reach the anterior border of the sternomastoid muscle. At this point it perforates the deep fascia, and leads to the formation of a cold abscess under the skin. Not infrequently, the skin over the abscess becomes thinned and breaks down, giving rise to a sinus.

Cold abscess formation may signify complete destruction of the offending gland, but caseous or calcareous fragments may be responsible for persistence of infection and may require removal.

### TUMOURS OF LYMPH VESSELS : LYMPHANGIOMA

A lymphangioma is similar to a hæmangioma except that its spaces and channels contain lymph. The tumour, which is often of congenital origin, results either from new formation of lymph spaces or vessels or from dilatation of those which already exist. Usually the tumour is completely isolated from the normal lymph channels, but in some cases communications are present. There are three chief varieties: capillary, cavernous, and cystic.

A *capillary lymphangioma* occurs most often in the lips, cheeks or tongue or in the skin and subcutaneous tissues and less often in muscles and internal organs. It gives rise to a localized nodular tumour, or causes diffuse enlargement of the part in which it is situated. For example, in the tongue it leads to one form of macroglossia. On section the tumour is composed of anastomosing channels or spaces lined by flat or cubical epithelium and filled with clear fluid containing a few lymphocytes. The stroma is composed of fibrous tissue. In a few instances, a hæmangioma and lymphangioma are combined.

A *cavernous lymphangioma* occurs chiefly in the skin, but sometimes in the intermuscular septa or in the mucous membranes where it may give rise to a circumscribed or diffuse tumour. It is composed of dilated lymph spaces which intercommunicate. The spaces are lined by flat endothelium and contain thin fluid or coagulated lymph. Hæmorrhage may occur in the tumour and thus create the appearance of a hæmangioma.

A *cystic lymphangioma* occurs chiefly in the neck, axilla and groin, occasionally in the sacral region or great omentum. Less frequent situations are the floor of the mouth, the liver and the suprarenal glands. The cyst is usually thin walled and multilocular and may reach a very large size. It may be present at birth or may appear soon afterwards.

In the neck the tumour is known as a *cystic hygroma*. It may be definitely circumscribed, but frequently it forms a ramifying mass which extends deeply between the muscles, and may even extend to the thorax or axilla. It may disappear spontaneously, but more often this is accelerated by infection of its contents.

### LYMPHOSARCOMA

A lymphosarcoma or reticulum cell sarcoma is a tumour of lymphoid tissue, and is believed to arise from the progenitors of the cells of

lymphoid tissue. It is characterized by rapid growth and a high degree of local malignancy. It occurs most commonly in young subjects and it progresses rapidly to a fatal issue.

The tumour may originate in a lymph gland or in any other collection of lymphoid tissue. Most frequently it arises in one of the glands of the neck or the mediastinum, or in the tonsil or the lymphoid tissues of the nasopharynx. In other cases it may arise in the mesenteric or retroperitoneal glands or in the lymphoid tissue of the gastrointestinal tract. Rarely it occurs in any tissue in which lymphoid tissue is present.

The tumour grows rapidly and attains large size. It is usually of pale colour and soft consistence, and is very liable to necrotic softening and hæmorrhage. It spreads from the site of origin, infiltrating surrounding tissues and involving other lymph glands in the vicinity. Subsequently more distant glands are affected, apparently by extension along lymph vessels and ultimately small metastases may develop in the liver, spleen or other organs. Microscopically, the normal architecture of lymphoid tissue is lost, and the tumour consists almost entirely of small, round, dark staining cells, supported by very scanty stroma. Sometimes larger cells of endothelial type are present, which are regarded variously as primitive lymphoblasts or as endothelial cells derived from the lymph cords.

In some cases the reticulum cells of the lymph sinuses are represented, and deeply staining argyrophil reticulum fibrils are a prominent feature (*reticulum cell sarcoma*).

Lymphosarcoma in the neck forms a bulky soft mass which becomes fixed to surrounding structures and may ulcerate at the skin. It originates usually in a gland of

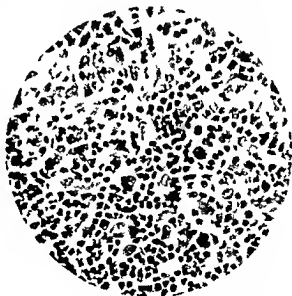


FIG 116. *Lymphosarcoma.* The tumour is composed of small round cells with hyperchromatic nuclei and of larger cells of endothelial type. A few malignant giant cells are present.

(Laboratory of Royal College of Physicians of Edinburgh)

the upper deep cervical group or in the tonsil, and spreads thence to involve the glands of the other side and those of the mediastinum or the axillæ. Lymphosarcoma in the mediastinum tends to spread diffusely in the mediastinal tissue planes and to invade the lung, and it may give rise to a fatal issue from pressure upon the trachea or great vessels. It may be remarked at this point that mediastinal lympho-

sarcoma is probably not so common as was supposed at one time, for many of these mediastinal growths are now known to be atypical carcinomata derived from the bronchi, and others are tumours of the thymus

Lymphosarcoma in the abdomen may arise either in a lymph gland or in the lymphoid tissue of the gastro intestinal tract. A growth arising in the latter situation occurs most often in the wall of the distal part of the ileum, less often in the jejunum stomach or colon. It arises usually in the submucous layer and infiltrates the gut wall diffusely, thickening it over a large area and ulcerating at the mucous surface. Sometimes multiple nodules, apparently independent, arise in different parts of the intestine

### LYMPHADENOMA (HODGKIN'S DISEASE)

Lymphadenoma or Hodgkin's disease is an affection of the lymphoid and reticulo endothelial tissues. It is characterized by painless enlargement of the lymph glands and spleen and by anæmia of secondary type. In some cases the lymphoid or reticulo endothelial tissues of the liver,



FIG. 117. Lymphadenoma

lung, bone marrow and alimentary tract are also involved. Generally it affects young adults, especially of the male sex, and it usually progresses during a few years and terminates fatally.

**The Lymph Glands.** The glandular enlargement is a constant, and generally the earliest sign of the disease. The enlargement is limited at first to the lymph glands in a single region and it may remain so limited during many months or even years, but later it affects

other groups of glands and eventually may affect lymphoid tissues in all parts of the body. The first glands to become enlarged are usually those at the root of the neck on one or on both sides. In others the glands in the upper part of the neck or in the mediastinum are affected first. Less commonly, the earliest site of the disease is in the glands of the axilla, groin, or retro peritoneal region.

The affected glands attain considerable size, and when situated within the thorax or the abdomen may give rise to pressure effects. Glands in the mediastinum may exert pressure on the large veins and give rise to venous engorgement and œdema of the face and neck, or they may press upon the trachea and embarrass respiration. Glands in the abdomen may cause obstruction of the alimentary tract or of the portal vein or, rarely, the common bile duct.

On cross section the lymph glands have a characteristic appearance. They are of a uniform homogeneous character, pinkish grey in colour, and elastic to the touch. At first they are of somewhat soft, fleshy consistency, later, they are firm and fibrous. The glands do not encase and never undergo calcification. There is no periadenitis, and consequently the glands remain discrete and non-adherent to surrounding tissues.



FIG. 118. Lymphadenoma  $\times 900$ . Note the endothelial cells and the characteristic giant cells.

Microscopically, the appearance varies at different stages of the disease. At first there is proliferation of all the specific cells that take part in the formation of a lymph gland, the reticulo-endothelial cells of the gland "corridor," the endothelial cells of the germ centres, and the lymphocytes which occupy the bulk of the gland. Many of the cells assume immature type, and large lymphocytes and eosinophil leucocytes make their appearance. At this stage giant cells of special type are usually present. Some of them are mononuclear cells, somewhat resembling endothelial cells, from which they probably take origin. Others are multinucleated cells which bear a striking resemblance to the megakaryocytes of the bone marrow.

In the late stages of the disease the microscopic appearance is



altered by the growth of fibrous tissue which infiltrates the whole gland and replaces the cellular elements

**The other Lesions** Whilst enlargement of the lymph glands is an invariable feature of Hodgkin's disease, involvement of other organs is less constant

The spleen is affected in most cases at some stage of the disease. It is enlarged sometimes considerably so. In some cases it is uniform and homogeneous in appearance, in others it is nodular, and the cut surface shows the presence of pale rounded masses somewhat resembling suet. Microscopically the changes are similar to those seen in the lymph glands.

The blood shows the changes characteristic of a secondary anaemia. In some cases there is a moderate leucocytosis and there may be an increase in the number of eosinophil cells.

The liver is involved in some cases and presents a diffuse cellular infiltration along the portal tracts. Rarely the bone marrow, the lungs and the submucous tissues of the stomach and small intestine show a diffuse cellular infiltration or even nodular swellings. Such nodules in the stomach or intestine may project into the lumen and may be mistaken for sarcoma.

*The cause of lymphadenoma* is not known. The disease has been regarded by many workers as a form of tuberculosis due to attenuated human or bovine bacilli. While it is true that in a small proportion of cases guinea pig inoculation of extracts from the affected glands yields a positive result this may be due to a coincident tuberculous infection and the negative results obtained in the great majority of cases must be regarded as conclusive evidence against this theory. The view that infection with the avian type of tubercle bacillus is responsible has also now been generally discarded.

In some respects lymphadenoma is comparable to the leukaemias and to lymphosarcoma and many observers regard it as a type of tumour formation allied to these conditions.

Lastly, there is the view that lymphadenoma is due to infection by organisms of low virulence. The attacks of pyrexia (Pel-Ebstein waves) that form such a characteristic feature of the clinical course give some support to this theory. Various workers have isolated streptococci, diphtheroid bacilli, and other organisms from the affected glands but their very multiplicity precludes conviction.

## SARCOIDOSIS

Under this title a motley of obscure diseases has gained shelter. The disease is fairly common and has attracted considerable interest on account of its obscure nature and the multiple and odd pathological lesions it may present. It may be latent, but it usually gives rise to a protracted illness which recovers spontaneously often with residual fibrosis in the affected organs.

The pathological features are mainly the result of proliferative changes in the lymphoid tissues like those in tuberculosis but always without caseation. The manifestations are most constant in the

lymph glands but the lymphoid tissue in the lungs the spleen and in the salivary glands and other risks may be affected. Skin lesions in the form of small papules on the face and limbs are present in half the cases. Bone changes are present in a small proportion.

The lymph gland enlargement is never more than slight and is always painless. One or several groups of glands may be affected the glands are discrete and freely movable and folliculoid deposits with epithelioid cells and scanty giant cells. The bone changes are commonest in the hands and feet and consist of well demarcated deposits of sarcoid tissue in the marrow of the phalanges.

The changes in the lungs may resemble peribronchial tuberculous infiltrations or miliary tuberculosis. The hilar glands alone may be affected.

Uveoparotitis Mikulicz's disease and possibly Still's disease are believed to be manifestations of sarcoidosis.

The underlying nature of sarcoidosis remains unsolved. It resembles tuberculosis and some cases ultimately succumb to that infection either in the primary or other sites. However, most cases show usually a negative Mantoux reaction and attempts at animal inoculation of biopsy material have not succeeded. Yet these features do not completely nullify a tuberculous origin of the disease and there is a growing body of opinion—circumstantial and factual—that pathologically sarcoidosis represents a form of tissue response to be expected in an individual with unusually high immunity and low sensitivity to tuberculous infection and the tissue response is proliferative as opposed to exudative.

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## CHAPTER XIII

### DISEASES OF THE SKULL AND BRAIN

#### THE CEREBROSPINAL FLUID

THE existence of a "third circulation," unsuspected until fifty years ago, is now clearly recognized. Cerebrospinal fluid, produced by the choroid plexus of the lateral and third ventricles, circulates through the ventricular system and over the surface of the brain, and is absorbed into the blood stream in the venous sinuses of the dura mater.

How the fluid is produced remains doubtful. The fluid has sometimes been regarded as an active secretion, for its composition signifies a remarkably selective process. Very few drugs reach the cerebrospinal fluid, and even the pigments of obstructive jaundice, which colour all transudates and many secretions, are usually withheld from it.

The fluid differs from every other bodily secretion, in containing the salts and sugars of the blood but practically no proteins. According to Mestrezat the fluid is a dialysate, escaping from the blood through the colloidal membrane formed by the cells covering the choroid plexus. All the contents of the cerebrospinal fluid are derived from the blood plasma, and salts, sugars, urea and diffusible organic substances such as alcohol, ether, or chloroform may pass into the fluid, but colloids are completely excluded. Moreover, the flow of cerebrospinal fluid seems to depend upon physical rather than vital influences for its pressure is regulated by the arterial blood pressure, and increases when venous stasis is brought about.

From the choroid plexuses the fluid passes through the ventricular system and escapes through the openings in the roof of the fourth ventricle, the central rounded foramen of Magendie and the two lateral slit like orifices of Luschka, to reach the subarachnoid space. Here it filters through the large subarachnoid cisterns, the cisterna magna on the dorsal surface and the cisterna pontis and its extensions ventrally. A small quantity of the fluid passes along the membranes of the spinal cord, but the larger portion percolates upwards over the surface of the brain. Finally it is absorbed into the venous sinuses, especially those over the cerebrum.

It is now well known that the fluid is absorbed into the blood principally through the *arachnoidal villi*. These are delicate structures composed of arachnoid mater situated in relation to the venous sinuses of the vault and the anterior and middle fossæ of the skull. They resemble small herniæ of arachnoid membrane, protruding through gaps in the dura mater and projecting into the lumen of a blood sinus. The villi are capped by meningocytes (endothelial cells of the meninges) and enclose channels continuous with the subarachnoid space, so that the cerebrospinal fluid is brought into intimate contact with the blood.

and is readily absorbed. In later life some of the villi, especially those related to the lacunæ of the superior sagittal sinus, become thickened and calcified—the Pacchionian bodies.

**Functions of the Cerebrospinal Fluid** In the jolts and jars of daily life the cerebrospinal fluid probably tends to protect the delicate nerve cells of the brain, insulating them and acting as a sort of water cushion. It is of interest to note that the fluid is most abundant around the part of the brain that it is most important to protect—the medulla. In pathological conditions the fluid is of value as an inert mobile tissue that can be displaced to make room for the cranial contents. Its most important function, however, is that of a vehicle for the excretion of the products of metabolism of nerve tissue, in this respect compensating for the absence of lymph. It probably acts also as the vehicle whereby the internal secretions of the pituitary gland reach the blood stream.

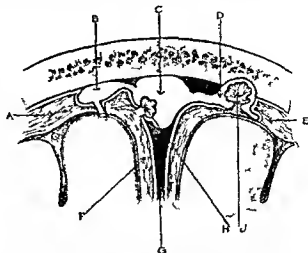


FIG. 119 Site of absorption of cerebrospinal fluid (A, E, F) subarachnoid space (B, D) lacunae laterales (C) superior longitudinal sinus (G) falx cerebri (H, J) arachnoid villi

(By courtesy of Professor J. Fraser and Mr. A. M. Dott.)

## HYDROCEPHALUS

Brief consideration of the physiology of the third circulation suffices to show that hydrocephalus may theoretically result from one of three processes, namely (1) increased secretion of cerebrospinal fluid beyond the limits of normal absorption, (2) obstruction to the flow in any part of its course, or (3) failure in the process of absorption. In practice, examples of the first process are rare, those of the third are uncommon, and the great proportion of cases are due to the second process and are thus examples of *obstructive hydrocephalus*. Obstructive hydrocephalus may occur in adult life, but is most common in infancy.

Hydrocephalus in adult life is usually due to the pressure of a tumour, rarely to obliteration of the ventricular foramina or of the subarachnoid space by adhesions following leptomeningitis. A tumour may obstruct the flow of cerebrospinal fluid directly or indirectly. A tumour of the acoustic nerve may press directly upon the mid brain and so constrict the aqueduct, or a tumour of the cerebellum may close the pathway at the fourth ventricle. More often, however, a tumour acts indirectly by displacing the brain stem towards the foramen magnum. This forms a "pressure cone" by impaction of the cerebellar tonsils and the medulla

in the foramen, and obstructs the outflow of cerebrospinal fluid from the fourth ventricle

Hydrocephalus in infancy may result from a congenital abnormality or may be due to obstruction to the fluid pathway by syphilitic meningitis or by adhesions following a birth hæmorrhage. The obstruction may occur in the aqueduct of Sylvius, the foramina in the roof of the fourth ventricle may be occluded, or adhesions over the surface of the

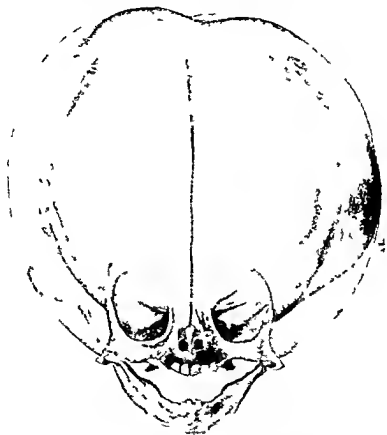


FIG 120 Hydrocephalus. The membrane bones of the skull are extremely thin and the fontanelles are of large size  
(Museum of Royal College of Surgeons of Edinburgh.)

brain may bar the progress of the fluid towards its area of absorption. Thus the obstruction may be intraventricular or extraventricular.

In the latter type not infrequently spina bifida co-exists, the spinal defect then acts as a safety valve, absorbing the excess of cerebrospinal fluid. Recognition of this coexistent deformity is of importance, for surgical repair of the spinal defect may aggravate the hydrocephalus.

In any type of hydrocephalus the end result is the same. The obstructed ventricles become dilated, compressing the tissues of the brain to a thin shell. The white matter is affected first and in greater degree, the grey matter resists for a much longer period. In childhood

incomplete ossification permits the skull to become enlarged and globular, contrasting remarkably with the tiny pinched face. The cranial bones separate widely and in the extreme stages parts of the skull are represented only by a thin stretched out membrane.

## INJURIES TO THE SKULL AND BRAIN

It is a commonplace that in head injuries the damage to the brain is often out of all proportion to the damage to the skull. Injuries which at first sight appear trivial, with no damage to the skull or only a small fissure, may prove fatal from their effect upon the brain or its vessels. Conversely, gross compound depressed fractures may, though uncommonly, be complicated by little evidence of injury to the brain. Fractures of the skull may cause tearing of cranial nerves or may provide a pathway for leakage of cerebrospinal fluid, and thus favour the access of infection, but in other respects their importance is small compared with the associated damage to the brain.

A head injury presents a complex physical problem. The effects are dependent upon the shape and size and speed of the striking force and upon the strength and elasticity and degree of fixity of the cranium. Thus at one extreme a blunt injury may cause prolonged unconsciousness but no permanent damage to the skull or brain, while at the other, a high velocity bullet may penetrate the brain or an airplane propellor may slice off a part of the skull without causing even momentary concussion.

Apart from war wounds, most injuries to the head are "blunt" injuries caused by the impact of a large mass. Such injuries commonly cause concussion and they may give rise to all degrees of bruising or lacerations of the brain and to extensive hæmorrhages, intracerebral, subdural or extradural.

**Concussion.** This state is characterized by three essential features, (1) sudden loss of consciousness, (2) widespread motor and sensory paralysis of variable duration, (3) subsequent complete recovery apart from retrograde amnesia for the events leading up to the injury.

Unconsciousness occurs immediately on receipt of the blow. When the concussion is slight there is merely transitory giddiness or momentary loss of consciousness, but when more severe the unconsciousness may be prolonged. The voluntary muscles and sphincters are relaxed, respiration is shallow and rapid, the pulse is small and quick, the pupils are dilated and, indeed, every vital activity is suspended.

In rare instances concussion accompanied by no other obvious injury has proved fatal, and in these cases at autopsy the only recognizable damage has been widespread minute hæmorrhages throughout the brain.

**The Mechanism of Concussion.** The brain is supported, as in a water bath, by the cerebrospinal fluid inside the closed cranial cavity. This disposition of the part, protective as regards the jars and minor injuries of daily life, has its own peculiar dangers when the skull is subjected to undue violence, for the force of the impact is transmitted, according to the laws governing hydrostatic chambers, rapidly to every part of the cavity.

Formerly concussion has been attributed to a sudden deformation of the skull—a flattening in the line of the force, or broadening in the other axis—which has been thought to produce a transitory anemia of the brain (Trotter) or a wave of pressure transmitted by the cerebrospinal fluid through the ventricles and impinging on the floor of the fourth ventricle (Duret).

The observations of Denny Brown and Russell make it necessary to modify these views. These workers have shown that in animals concussion is produced most readily if the head is not fixed, *i.e.*, is capable of being displaced at the moment of impact. From this it must be concluded that concussion is due to a sudden change in velocity (acceleration or deceleration) rather than to an increase of intracranial pressure. The velocity of the force at the moment of impact is thus of paramount importance, and if the impact is damped down by cushioning the risk of concussion is greatly reduced.

It seems probable that the actual lesion in concussion is a "molecular disturbance" of the neurones caused directly by the physical stresses due to the impact. Most of the characteristic features of concussion can be attributed to a transitory paralysis of this sort affecting particularly the hypothalamus and brain stem. Even the unconsciousness or, as he prefers to call it, parasomnia, has been attributed by Jefferson to brain stem paralysis.

**Contusions and Lacerations.** These injuries vary in degree up to the most severe. They are most extensive at the site of impact of the blow, and at the opposite pole, from percussion of the brain against the skull at this point (*contre-coup*). The same mechanism may lead to damage to the brain close to the dural partitions, and the nerve tissue close to the ventricles is often affected. The damaged areas become softened and disintegrated and may bleed. Blood may percolate through the meshes of the pia arachnoid or even escape into the subdural space, but more frequently it is restricted to small areas in the brain itself.

When the damage is extensive it may give rise to focal paralytic lesions from destruction of nerve tissue, but such gross damage is unusual. Minor contusions and lacerations owe their chief danger to the coincident localized hemorrhages and reactionary edema of the brain. If this stage is survived, the damaged tissues may become sclerotic from neuroglial proliferation, and this sclerosis may subsequently give rise to after effects.

**Edema of the Brain.** The contused brain like any other bruised tissue becomes swollen with extravasated blood and edema fluid. In most cases the edematous swelling is limited to the immediate vicinity of the focal lesions, but in severe injuries it may be so extensive as to cause an increase in intracranial tension and interfere with the circulation of blood and cerebrospinal fluid.

The state of "cerebral irritation" is generally attributed to edema of the brain, though the evidence for this view is not altogether convincing. This state appears shortly after recovery from the initial concussion and may persist for a few days or considerably longer. Usually it reaches its maximum within forty-eight hours after the

injury The cerebral condition is reflected in the whole state of the patient, who lies curled up on his side, avoiding the light and resenting all interference The mental state varies from irritability and drowsiness to delirium and even mania, the more excitable states usually supervening at night During quiet phases there is a curious state of submerged consciousness, for although apparently insensible the patient may respond to persistent questioning, but with a long reaction time, slowness of thought, and defective memory.

**Intracranial Hæmorrhage.** Intracranial hæmorrhage of traumatic origin may arise from rupture of a vessel either in the meninges or in the brain Intracerebral hæmorrhages are very common following bruising or laceration, but they are usually small, or overshadowed by other lesions

**Extradural Hæmorrhage.** Extradural hæmorrhage, though uncommon, is familiar clinically, for it gives rise to a fairly characteristic train of symptoms and signs It follows rupture of a meningeal vessel, often the main stem or a major branch of the middle meningeal artery, which is punctured or torn by a fracture of the inner table The onset of bleeding is delayed by the initial collapse and low blood-pressure of the concussion period, and its progression is slow due to the adhesion of the dura mater to the bone, and for these reasons there is usually a latent period, free from pressure symptoms Since the dura is firmly attached at the base of the skull the blood spreads principally towards the vault, and also antero posteriorly As the hæmatoma increases it compresses the adjacent parts of the brain and increases the intracranial tension Its effects are at first and principally restricted to the brain close to the hæmorrhage, and only later do they become generalized The brain abutting on the site of hæmorrhage is at first engorged from venous stasis, and is "irritable", later, this part of the brain becomes paralysed, while a zone of "irritability" spreads progressively to other parts

In typical cases these pathological processes may be recognized clinically After the initial concussion and before the bleeding has progressed far, there is a latent period, free from symptoms Then, in a few hours or, exceptionally, a few days, there develop irritative phenomena due to the venous stasis, related principally to the affected side Later there are paralytic disturbances, at first localized, later spreading as more and more of the brain is affected (*compression of the brain*) Monoplegia, hemiplegia, or sensory loss occur, and paralysis of the palate leads to stertorous breathing The pupil of the affected side becomes dilated, whereas its fellow, affected by the irritative zone of venous stasis, is contracted Generalized paralytic lesions and deepening coma lead to death

An instructive feature of the late stage of compression of the brain is the character of the pulse, which is full, bounding and of high tension This is known as the "compression pulse" The vital centres of the brain stem must at all costs receive their proper nourishment, and to ensure this they are furnished with a remarkable compensatory mechanism When the advancing effects of cerebral compression approach the medulla, that most delicate vital centre, the vasomotor centre, is the first to respond by becoming more susceptible to stimu



lation and emits impulses which lead to vaso-constriction of peripheral blood vessels. This has the effect of raising the blood pressure, and since the cerebral arteries, being independent of vaso-constrictor control, do not participate, the result is an increased flow of blood to the medulla and consequent improvement of the nutrition of the vital centres. Thus the "compression pulse" is a protective phenomenon.

**Subdural and Subarachnoid Hæmorrhages** Blood may accumulate either in the subdural space or in the meshes of the pia arachnoid. The blood may come from a meningeal artery or a venous sinus, or from veins or arteries near the surface of the brain. A common source is from one of the cerebral veins as they enter the tributaries of the superior longitudinal sinus, for these are short venous trunks passing perpendicularly from the mobile brain to the fixed dura mater. The hæmorrhage is most likely to follow a blow on the back of the head, in which the brain is suddenly thrown forwards within the cranial cavity. In blows directed from one side of the head, the brain is cushioned to some extent by the falx cerebri, and consequently is less apt to tear the veins.

Arterial hæmorrhage usually is too rapidly fatal to have much significance. Venous bleeding progresses slowly, after a free interval due to the initial shock. If the hæmorrhage is not sufficiently severe to lead to death, the blood clots, forming a hæmatoma. Small clots are absorbed, but large ones tend to persist.

**Chronic Subdural Hæmatoma** Such a collection of blood clot is found most often over the parietal region, a short distance from the midline. Within a few days it becomes enveloped in membranous adhesions derived from the arachnoid mater. This membrane contains numerous reticulo-endothelial cells or *meningocytes*, which phagocytose the hæmoglobin from the blood clot, and even convert some of it into bile pigment, thus imparting a greenish yellow or coffee colour to the affected region.

Eventually the blood clot becomes liquefied, and forms a cyst—*traumatic subdural cyst*. Such cysts are not intimately connected with the brain or dura, and may with care be shelled out. The outer parts of the cyst become organized and fibrotic, the centre becomes liquefied, and its pigment undergoes absorption. Cholesterol crystals may be deposited in large numbers. Such a cyst sometimes tends to increase in size through the accumulation of fluid, and may give rise to the signs of an intracranial tumour. Its wall may become calcified and thus be evident in radiographs.

### Sequelæ of Injuries to the Brain

Any injury to the brain, from a mild concussion to severe lacerations, may occasionally be followed by untoward sequelæ. Headache, giddiness, tinnitus and ill-defined alterations in disposition are the most frequent. Traumatic neurasthenia may follow more severe injuries. It is characterized by an alteration of the mental attitude with instability, incapacity for intellectual effort, and attacks of excitement alternating with depression.

Traumatic epilepsy is a rare sequel, attributable to irritation of

the motor cortex secondary to patchy gliosis in the lacerated area. Traumatic insanity is also a rare sequel which occurs in persons with an inherited tendency towards mental instability.

The relation of post traumatic disturbances to a defect in the bones of the cranium is a problem of great importance to the surgeon. Often the headache appears to be centred round the defect, the patient has an unpleasant consciousness of weakness at this point, or there may be local pain, and appreciation of variations in intracranial tension, of which the normal person is unconscious. In some such cases it appears as though the defect itself is responsible for the symptoms, for closure of the gap by a bone transplant may bring relief. Usually, however, adhesion of membranes to the brain at this point and gliosis spreading deeply through the brain are the underlying factors.

In addition to the sequelæ mentioned above, there are certain complications due to rupture of cerebral nerve tracts at the time of the injury. In this category are glycosuria, polyuria (from damage to the hypothalamic region), loss of sight, hearing or smell.

*Intracranial aerocele* (pneumocephalus) may also occur. This rare condition is characterized by the presence of an air containing cavity within the skull. In the common form, the aerocele lies within the substance of the frontal lobe, and it may be so large as to occupy the entire frontal lobe and extend back into the parietal lobe. In some cases, the air occupies a portion of the subdural or subarachnoid space. It may even gain access to the ventricles, either primarily or following rupture of an aerocele in the frontal lobe.

In the great majority of cases the aerocele results from a fracture of the cranium involving one of the air sinuses—the frontal sinus most often, the ethmoid, sphenoid or mastoid sinuses rarely. At the time of the fracture the subjacent dura mater and arachnoid are torn, and a narrow track is formed leading from the air sinus into the brain. When the patient coughs or sneezes (or swallows, in the case of the mastoid air cells), the increased pressure within the sinus forces air into the substance of the brain.

In a few cases the bone defect has been caused by inflammatory erosion of the sinus wall, for example, in mastoiditis or ethmoiditis. It is possible that occasionally an aerocele may result from the action of gas forming organisms, for example, in a brain abscess.

An intracranial aerocele generally develops several days, or even a few weeks, after injury. In the common frontal type it is associated with repeated sneezing and sometimes with the discharge of cerebrospinal fluid from the nostril. As the aerocele increases in size the intracranial tension rises, and leads to headache, vomiting, drowsiness or delirium, and finally coma. In 50% of cases the issue is fatal, either from intracranial pressure or from superadded infection.

### Injuries to the Skull and Cranial Nerves

The skull may be fractured at the site of impact of a blow, from its direct violence, or at some distant part from secondary stresses set up in the bones. The nature and extent of the fracture depend upon the size of the injuring object as well as upon the magnitude of the force.

A small object inflicts a localized fracture at the point struck. The fracture may be compound, comminuted or depressed, and it may be given various descriptive names—indentation, pond, gutter, punctured, etc. Such fractures are commonest in the vault of the skull. Rarely a pointed object may pass through the mouth or nose and cause a direct fracture of the base or pass through the orbit and lead to damage of the orbital plate. Where such an injury is caused by an object of small calibre, the wound of entry may be so slight as to escape the most careful inspection.

A large object, inflicting violence over a wide area of the skull damages it by a different mechanism. There may be local damage at the site of impact, but, in addition, abnormal stresses and strains are set up through the whole skull. The base, the least elastic portion, gives way first, and fissures appear, which may extend widely, usually in a transverse direction or obliquely. Not infrequently the fissures radiate in several directions, and they may cross the mid line at the base.

The cranial nerves may be injured in fractures of the base of the skull, particularly of the anterior and middle fossæ. Nevertheless it is remarkable how often the nerves escape injury, even in very extensive fractures. Often the line of fracture avoids the nerve trunks, which are surrounded by dense bone and so are relatively resistant. Fibres of the olfactory tract may be torn in an injury to the cribriform plate, the optic nerve is liable to be damaged as it lies in the optic foramen, injury to the petrous bone may rupture the abducent nerve, the facial and acoustic nerves may be injured as they lie in their bony canals.

Healing of a fracture in the membrane bones of the skull takes place by fibrous union. Usually bony union does not take place, and there is no formation of callus at the seat of fracture. Occasionally, after a long interval, there is a certain amount of ossification between the fragments where the fracture crosses a suture line, but the new bone is always very scanty. The lack of new bone formation is generally attributed to the fact that osteoblasts are absent from the bones formed in membrane. Similar failure of ossification occurs at the site of a compound comminuted fracture, the edges of which remain clearly defined and little altered after a period of years.

paranasal air cavities, or it may arise as a complication of a compound fracture of the skull. Not infrequently it is due to spread of infection from a septic focus in the lip, nostril, or orbit. Rarely intracranial suppuration follows infection from a distant septic process. Intrathoracic infections such as bronchiectasis or pulmonary abscess are especially apt to involve the brain, presumably owing to the ease with which septic emboli set free in the pulmonary veins may be transported to the cerebral arteries.

**Pathways of Infection.** Infection may reach the intracranial structures by the following routes —

(1) By continuity of tissue, *e g*, extradural abscess secondary to otitis or compound fracture of the skull

(2) By the arterial blood stream *e g*, brain abscess secondary to pyæmia or thoracic infections such as bronchiectasis

(3) By the venous blood stream, *e g*, sinus thrombosis secondary to carbuncle of the lip

(4) By special regional pathways such as the olfactory perineural sheaths, *e g*, meningitis secondary to fracture of the cerebroform plate

**Extradural Abscess** This is attributable almost invariably to spread of infection from some local lesion. Most often it follows suppurative otitis media or infection of the mastoid air cells, or it may occur as a complication of compound fracture of the skull, osteomyelitis of the cranial bones, or infections of the scalp.

In the common form secondary to ear disease the abscess cavity is of small size, contains very little pus, and is surrounded by an exuberant mass of granulation tissue, which lies between the dura mater and the bones of the skull. The abscess gives rise to constitutional effects, but since its size is small there is rarely evidence of increased intracranial tension or of focal lesions from pressure on the brain. Sometimes, however, papilloedema (optic neuritis) occurs.

Extradural abscesses following compound fracture vary in severity with the virulence and the variety of the infection. Not infrequently they appear several weeks after the injury and grow slowly to large size, giving rise to increasing toxæmia and to signs of an increased intracranial pressure. If the infection is virulent, and particularly if the dura mater has been damaged at the time of fracture, the leptomeninges may become involved.

When the skin over an extradural abscess is unbroken, there sometimes develops a hard, tender, localized swelling of the soft parts (Pott's puffy tumour), an inflammatory oedema comparable to that seen superficial to any acute suppurative process, and without other pathological significance.

An extradural abscess may resolve, but if untreated is apt to extend beyond the reactive zone of granulation tissue and to lead to subdural infection, leptomeningitis or abscess in the brain.

**Acute Leptomenigitis** This may, like extradural abscess, follow local infective lesions, or it may follow infection from some distant source. The latter type, exemplified in meningococcal meningitis and in the meningitis of pneumonia, septicæmia or other disease, does not require consideration here.

Local infection of the leptomeninges is most likely to arise where the dura mater has been damaged, as in a compound fracture or by a penetrating wound but it may occur with the dura mater intact. The condition is grave, for the whole subdural space is usually invaded. Occasionally, however, if the infection is less virulent, adhesions form and lead to resolution of the disease or to a localized subdural abscess.

**Thrombophlebitis of the Venous Sinuses** This is a grave and often fatal affection. The channel most often affected is the *lateral sinus* which owes its susceptibility to its close relation to the middle ear. The disease usually follows osteomyelitis of the mastoid bone secondary to otitis media, and the sinus may be infected by direct continuity or along one of its small tributary veins. As a result of the infection the endothelial lining of the sinus becomes inflamed and thickened, and thrombosis occurs blocking the lumen. The thrombus being infected undergoes suppuration and softening and consequently is very apt to break down and to cause general pyæmic dissemination. The thrombosis may extend down the internal jugular vein which may then be felt as a firm tender cord in the upper part of the neck. Abscesses may form in the soft tissues around the vein and the cervical lymph glands are enlarged and tender. The infection may spread in other directions and lead to meningitis and cerebral abscesses.

The *cavernous sinus* may be infected from the lateral sinus or from septic lesions in the soft tissues of the face or orbit, by thrombosis spreading along the angular vein or by way of the pterygoid venous plexus. It is to this complication that insect bites, erysipelas, boils and carbuncles in the region of the upper lip and cheek owe their especial danger. Since the two cavernous sinuses are directly connected across the mid line the infection rapidly becomes bilateral. Obstruction of the venous pathway and the local effect of the intense inflammation combine to cause great congestion and œdema within the orbit and in the eyelids and face. The infection may lead to paralysis of the third, fourth and sixth cranial nerves which lie in or on the wall of the sinus and thus give rise to ptosis, squint and ophthalmoplegia. The infection if unchecked tends to spread along communicating venous channels and in all but a few cases is rapidly fatal.

The *superior sagittal sinus* is only rarely affected and then usually from septic processes in the skull or scalp. Its pathological features do not differ from those seen in other sinuses.

**Abscess of the Brain.** An abscess in the brain may be due to direct bacterial invasion from some local suppurative process or to hæmatogenous infection from some distant source. The former is by far the commoner mode of origin.

*Abscesses due to local suppuration* are most often attributable to disease of the middle ear and the abscesses are situated in those parts of the brain that lie nearest to the primary focus, namely, the temporal lobe or cerebellum. An abscess in the temporal lobe is usually situated in the white matter of the centrum ovale. It is generally attributable to spread of the infection through the tegmen tympani and there is often extradural and subdural suppuration in the same region. In other

cases there is no evidence of direct extension, and it may be presumed that the infection has been carried along communicating veins. A cerebellar abscess, which usually lies on the same side as the diseased ear, is often secondary to phlebitis of the sigmoid portion of the lateral sinus, to which it is closely related.

Much less often the cause of the abscess is to be found elsewhere than the middle ear. Suppuration of the frontal sinuses occasionally leads to abscess in the frontal lobe, and rarely septic osteomyelitis of one of the skull bones has a similar sequel. Injuries to the skull and brain provide a portal of entry for organisms, or infection may be introduced at the time of injury, and if foreign bodies such as portions of clothing or fragments of shrapnel are also introduced an abscess is especially likely to occur.

The character of the abscess depends upon the virulence of the infection. If acute, the abscess is ill defined, and is more correctly regarded as a spreading suppurative encephalitis. A chronic abscess, which is more common, becomes surrounded by a capsule of firm fibrous neuroglial tissue, and may remain latent for many weeks. The abscess is usually single, and of small size. Its purulent content is usually thick, foul, and of greenish yellow colour, but it may be dark brown from admixture with broken down blood clot. Staphylococci, streptococci or pneumococci may be present, but often the pus appears sterile when tested by ordinary cultural methods.

*Metastatic abscesses*, due to hæmatogenous infection, are not infrequent in the course of general pyæmic and septicæmic states, and are then usually small and multiple. Abscesses may, however, occur quite apart from general pyæmia, and in cases where there is no other evidence that the infection has gained the blood stream. This occurs most often as a complication of intrathoracic suppurative diseases, bronchiectasis, abscess of the lung, or chronic empyema, and it constitutes one of the risks of operations on infective lesions within the thorax. It seems likely that the special relationship of thoracic disease to brain abscess may be explained simply upon the anatomy of the circulation, for minute infected particles set free in the pulmonary veins pass directly to the systemic circulation. Not infrequently abscesses following thoracic disease are single. They are situated most often in the cerebrum, and since the infection is virulent they usually progress rapidly to a fatal issue, often by rupture into the ventricles.

## INTRACRANIAL TUMOURS

Intracranial tumours include tumours arising from the brain itself, from its membrane, from the pituitary gland or from the acoustic nerve, as well as some rare varieties. Tumours from these sources vary greatly in their morphology, incidence, and life history. Many are rapidly growing, infiltrating tumours, unresponsive to any form of therapy, however early and intensive, others, on the contrary, grow slowly, and are amenable to surgical treatment.

The work of Cushing and his associates has done much to dispel the earlier fatalistic attitude towards brain tumours. An intracranial

neoplasm does not now inevitably presage death, and in an appreciable proportion of cases a complete eradication may be accomplished.

Of this latter group the outstanding example is the meningioma, which if accessible may be extirpated completely and with safety. Tumours of the acoustic nerve also may be removed though the operation has its special dangers. Some of the tumours of the glioma group react well to palliative measures, so that the fatal issue may sometimes be postponed for many years.

It is of obvious importance to have a full appreciation of the various types of intracranial tumour and of the secondary disturbances which they may set up. These naturally vary in form and degree, but all types of growth tend, from their situation within the cranial cavity, to have certain effects in common. In general, they may affect (1) the brain, whether by compression, invasion, irritation, hæmorrhage or œdema, (2) the intracranial circulation, of blood or cerebrospinal fluid, (3) the skull, by erosion or invasion, and (4) the spinal cord, by descending degenerations of the nerve tracts. A few tumours may, in addition, affect the meninges, by invasion or implantation. Rarely, the more malignant forms may invade even the soft parts outside the skull, and this is especially apt to occur after a decompression operation. Intracranial tumours practically never metastasize.

The relative frequency of different varieties of tumours is indicated by Cushing's statistics, taken from an extensive series of 1,140 cases. In 43% of these, the tumour originated in the brain itself (various types of glioma, including "gliosarcoma" and "sarcoma"), 10% were pituitary tumours, 12% meningioma and 9% tumours of the acoustic nerve. Miscellaneous tumours, including congenital and metastatic growths, made up the remaining 17%.

### MENINGIOMA (Dural Endothelioma)

A meningioma is a simple tumour of slow growth, which is dangerous to life only by reason of its situation in the closed cranial cavity. It grows from the arachnoid mater (not, as was formerly believed, from the dura mater), and it seems probable that in most cases it originates from the arachnoidal villi which lie in relation to the large venous sinuses (*see p. 260*).

A meningioma is situated most often in the anterior and middle fossæ and on the superolateral surfaces of the brain. By reason of its slow growth, which permits compensatory changes in the bulk of the brain, it may attain considerable size, and at the time at which operation is performed it may be the size of a golf ball or even larger. Often the tumour is closely related to one of the large venous sinuses of the meninges, and often it is extremely vascular. Moreover, the vessels in the meninges and bone adjoining are frequently dilated, and consequently hæmorrhage at the time of operation may be profuse. Occasionally the tumour is less vascular and more fibrous, and it may then become calcified (*psammoma*).

A meningioma may extend deeply towards the brain or superficially through the dura mater and the skull. In extending deeply

it indents and displaces the brain but never invades it, and consequently when accessible it may be enucleated entire. Sometimes it is sessile, and is attached to the arachnoid mater by a broad base, but even when pedunculated and almost buried in cerebral tissue it always retains a definite capsule. The dura mater superficial to the tumour is first thickened by reactionary fibrosis and later invaded, and eventually the cranial bones also are affected.

The effects of a meningioma upon the overlying cranial bones are characteristic and important. The bone is sometimes invaded by tumour cells, but more commonly it undergoes changes from peri-



Fig 1-1 Meningioma (dural endothelioma). The tumour derived from the arachnoid mater has compressed and indented the brain but has not invaded it. Note the lobulated character and the vascularity of the growth. (After Cruevellier)

neoplastic hyperæmia. At first there is a simple erosion, so that a cup-like depression, sometimes bounded by projecting osteophytes, appears on the inner table. Later there is often some reactionary new bone formation on the outer table, forming a hard, smoothly rounded swelling under the scalp. Less often bone is formed in perpendicular deposits which resemble the "sun ray" spicules of periosteal sarcoma. Seen in a radiogram such an appearance is apt to suggest the presence of a primary bone tumour and the underlying meningioma may escape recognition.

Microscopically, a meningioma is composed of elongated, spindle-shaped cells somewhat resembling fibroblasts set in a matrix containing collagen fibrils and hyaline material. Commonly the cells



have a whorled arrangement, often around a central blood vessel. Larger cells of endothelial type may be present. Often the blood vessels are large and numerous, and there may be areas of hemorrhage. In some of the less vascular tumours there are spherical bodies com-

posed of concentric laminae infiltrated with calcium (*psammoma bodies*)

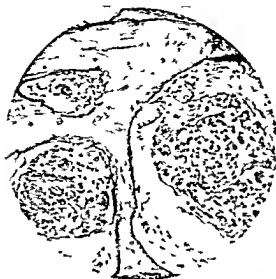


FIG. 122. Meningioma (dural endothelioma) penetrating the skull.  $\times 100$ . The tumour is composed of solid masses of cells arranged in whorls. The cells have the general character of endothelial cells. Near the centre of the whorls they are somewhat spindle shaped, and in other parts they are larger and more rounded.

The course of a meningioma is characterized by slow and, for the most part, symptomless growth. In approximately half of the cases there is a history of an injury, often definitely localized to the affected part of the skull. The first and for a long time the only sign may be some local disturbance, such as pain of a dull aching character localized to the affected region, or unilateral headache. Sometimes the inward growth of the tumour may give rise to focal signs such

as epileptiform convulsions or, if the tumour lies at the base, an ocular paresis. In other cases the presence of a bony swelling under the scalp may be the revealing sign. In radiograms the changes described above may be recognized, and, in addition, if the tumour is very vascular it may be possible to see dilated vascular channels in the bones.

### THE GLIOMA GROUP

This term has been applied to the tumours hitherto called gliosarcoma and sarcoma and to other lesions, as well as to the simple form of glioma, for it is now recognized that all these tumours, whatever their appearance and behaviour, are derived from the cells of the supporting fabric of the brain, the neuroglia. The neuroglia, like the actual nerve cells, is an ectodermal structure, and it is therefore incorrect to label its tumours sarcomata. True sarcoma is extremely rare, for practically the only mesodermal tissues in the skull are the blood vessels and their supporting framework.

In the past two decades there have been many additions to our knowledge of the pathology and life history of gliomata. On the one hand, improvements in the staining methods applicable to nerve

tissues, which have been introduced especially by members of the Spanish school of neuropathologists, have rendered possible an accurate appreciation of the histology of brain tumours, and, on the other hand, the widespread adoption of surgical measures in this field has given a great impetus to fuller investigation

### Classification of Gliomata

Bailey and Cushing have emphasized that in brain tumours, as in tumours elsewhere, the more primitive the predominating cell the more malignant is the tumour's behaviour. Tumours composed of cells resembling adult neuroglia cells are slow growing, and but for their peculiar situation would be non malignant, tumours composed of primitive cells grow fast and kill rapidly. The cells of the neuroglia in their development in the embryo undergo many changes of shape, form and staining reaction, and in tumours the cells may revert to any of these primitive forms. Thus it is possible to classify a tumour according to the degree of reversion of its predominant cell type, and the greater the reversion the more malignant the tumour.

This is the rational basis of Cushing's classification. It has evoked much adverse criticism on various pathological grounds, and particularly on the grounds that few brain tumours conform strictly to type, many show several different stages of cell differentiation, and many cannot be classified exactly in any of the recognized groups, but in spite of these criticisms there can be no doubt that the classification represents a great advance upon any previously attempted. For a proper understanding of its basis it will be necessary to consider briefly the development of the neuroglia.

**Development of Neuroglia.** Practically all the tissues of the central nervous system are derived from ectoderm. At the dorsal surface of the early embryo there appears a raised "neural plate," and this is hollowed out as the "neural groove," and later depressed below and completely separated from the skin surface. This is the primitive brain and spinal cord, and at this stage it is represented by a tube, lined by a single layer of epithelial cells derived from the surface ectoderm, the *neural or medullary epithelium*. Rarely the cells of a tumour revert to this primitive type, and the tumour is correspondingly malignant (the so called medullary epithelioma).

From this medullary epithelium there develop both the nerve cells proper and the supporting framework or neuroglia. The nerve cells and their immediate progenitors so rarely give rise to tumours that their development need not be considered further. Almost all brain tumours arise from glial tissues, and the development of the glia must therefore be studied in more detail. The primitive neuroglia cell is the *spongioblast*, an elongated, somewhat spindle-shaped cell that can be identified by its staining reactions with gold sublimate. Cells of this type are frequently seen in the common malignant glioma (gliosarcoma) and this tumour may therefore be called a *spongioblastoma*.

From this spongioblast stage the developing neuroglia cell undergoes

various modifications and eventually attains the adult form the *astrocyte*. This is a star-shaped cell with long branching spidery processes one of which the "sucker foot" is attached in close relation to a capillary blood vessel, whence its nourishment is derived. Astrocytes predominate in the simple glioma, which may therefore be called an *astrocytoma*. Two types of astrocyte are recognized protoplasmic

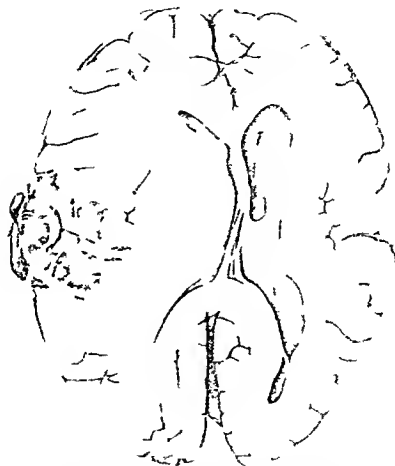


FIG 123 Glioma of the cerebral cortex. The tumour has extended to the surface of the brain and has compressed the lateral ventricle

(Department of Surgery University of Edinburgh)

astrocytes and fibrillary astrocytes and either may predominate in a simple glioma or astrocytoma.

One further cell requires to be mentioned--the *indifferent cell* or *medulloblast*. This is a small round or carrot shaped dark-staining cell. Its origin and function are not clear but it seems probable that it is derived from an original cell of the medullary epithelium and that it is bipotential able to form either nerve cells or neuroglia. It is con

sequently of primitive type, and its tumours, which arise most often in the cerebellum, are exceedingly malignant (*medulloblastoma*)

Lastly, there are two other structures from which tumours may occasionally arise, the pineal gland and the ependyma or lining membrane of the ventricles. Both of these tissues arise from spongioblasts at an early stage in the development of the brain, and the tumours arising from them may be regarded as gliomata with special characteristics

### Types of Glioma

The common tumours of the glioma group fall into three classes, distinctive both in morphology and clinical course. Formerly they were known respectively as glioma, gliosarcoma and sarcoma. Since "sarcoma" is inadmissible for tumours of ectodermal origin it is proper that these terms should be superseded, but it is by no means easy to replace them. The following classification may be adopted —

- (1) Glioma of slow growth    astrocytoma (simple glioma)
- (2) Glioma of rapid growth    spongioblastoma (gliosarcoma)
- (3) Glioma composed mainly of small round cells    medulloblastoma (sarcoma)

In addition, there are rare tumours arising from the pineal body, the ependyma, and other tissues

- (1) Glioma of Slow Growth    Astrocytoma (Simple Glioma)    This

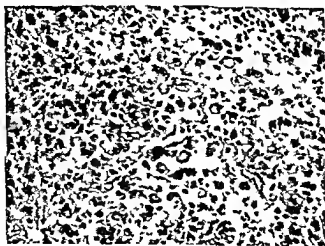


FIG 124. *Astrocytoma*. Small star shaped cells and many larger cells of protoplasmic type are seen. The fibrillar processes are evident.  
(Department of Pathology University of Glasgow)

tumour is composed mainly of adult neuroglia cells or astrocytes. It is the commonest neuroglial tumour, and it is relatively benign in the pathological sense and of slow growth. It occurs at any age and is common in the frontal lobes and in the cerebellum, less frequent in the other parts of the cerebral hemispheres. In adults the frontal lobes are

affected most commonly, whereas in children the cerebellum is the commonest site. The tumour forms a fairly firm mass of indefinite outline, merging indistinctly into the surrounding white matter of the brain. It is usually pale and relatively avascular, and is therefore liable to central degeneration from necrosis. This may proceed, especially in the cerebellum, to the formation of a *gliomatous cyst*, a rounded, smooth walled space of considerable size, containing clear straw coloured fluid. Sometimes the cyst may replace almost the whole tumour, and only a few tumour cells remain in the cyst wall.

Microscopically, the tumour is composed principally of adult astrocytes, which are recognizable in sections prepared by the gold

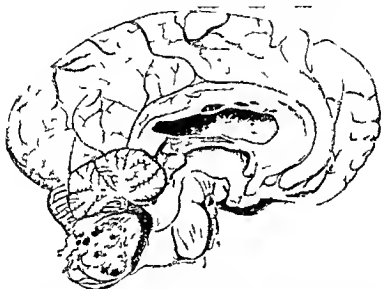


FIG. 12a. Glioma arising from the roof of the fourth ventricle. The tumour has displaced the cerebellum and has given rise to a considerable degree of hydrocephalus.

(Department of Surgery, University of Edinburgh.)

sublimate or other suitable methods as star shaped cells with elongated branching processes. The intercellular substance varies in amount and may be clear or traversed by numerous fibrils. Vessels are few and well formed, and mitotic figures are scanty. The whole appearance often may resemble adult neuroglia tissue and it may sometimes be difficult to distinguish the tumour from the surrounding white matter.

Tumours of this class are of slow growth, and if the dangers of increased intracranial tension are overcome by a timely and suitably placed decompression opening the fatal issue may be postponed for a considerable number of years. In Cushing's series the average survival period was almost six years.

(2) *Glioma of Rapid Growth. Spongioblastoma (Gliosarcoma)*. This tumour, almost as common as the first type, differs greatly in appearance

and behaviour. Its predominant cell is the spongioblast, the most immature cell of the neuroglia series, and the tumour is correspondingly malignant. It commonly affects adults between the ages of forty and fifty, but may occur at any age from ten to seventy years. The frontal lobes are the most commonly affected, less often other parts of the cerebrum. The tumour forms a bulky soft vascular mass, very liable to hemorrhage and to central necrosis. It invades the surrounding cerebral tissue and destroys it. Often the tumour appears to be encapsuled, but this appearance is misleading, for the capsule, which consists of brain tissue compressed by the rapidly growing tumour, itself contains malignant cells. The tumour usually



FIG. 126. Malignant glioma (spongioblastoma).  $\times 275$ . The tumour is derived from glia and it reproduces the primitive neuroglia cells or spongioblasts, large, darkly staining, spindle-shaped cells terminating at one or both poles in wavy processes.

does not invade the meninges, but in rare cases after an exploratory operation it may extend and involve the soft tissues of the scalp and neck. It does not metastasize to distant parts. A most important effect of the tumour is to give rise to widespread vascular changes and oedema in the brain. This oedema is one of the important factors leading to the early fatal issue.

Microscopically, the tumour is very cellular, and very pleomorphic. There are round and spindle-shaped cells of various sizes, so that

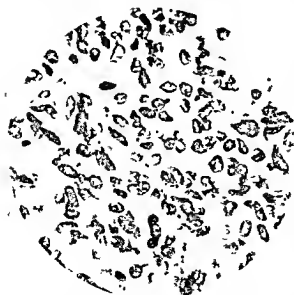


FIG. 127. Medulloblastoma.  $\times 460$ . A malignant tumour of the cerebellum, derived from neuroglia, and reproducing primitive glia cells of medulloblast type.

the growth resembles a rapidly growing mixed-cell sarcoma. Often giant multinuclear cells are present, and there may be syncytial masses. Mitotic figures, often irregular in form, are common. The tumour is very vascular and there are usually areas of degeneration and hæmorrhage. The high malignancy of the tumour is reflected in the post-operative survival rate, which in Cushing's series averaged twelve months. Decompression relieves the intracranial tension but has little effect on the cerebral œdema, and operation, therefore, often gives little benefit.

(3) *Ghoma composed mainly of Small Round Cells*. Medullo-blastoma (Sarcoma). This tumour, the third member of the ghoma group, is much less common than those already described, and it has been recognized as a distinct type only through the work of Bailey and Cushing. It seems probable that formerly it was often regarded as a small round-cell sarcoma. It is a tumour of childhood, and almost always arises in the cerebellum, either in the vermis or in one of the lateral lobes or in the roof of the fourth ventricle. The tumour has a remarkable tendency to disseminate along the meninges, and numerous secondary growths may cover the surface of the hind brain (sarcomatosis of the meninges), often obscuring the primary lesion. It is a rapidly growing tumour, and, from its position close to the fourth ventricle, it is very apt to cause hydrocephalus by obstructing the cerebral aqueduct. The tumour is very responsive to irradiation, and adequate exposure to X rays or radium may effect a remarkable relief of pressure symptoms.

Microscopically, it is very cellular. The cells are small, and round or carrot shaped, with deep-staining nuclei and scanty cytoplasm, and in its whole appearance it resembles a round-cell sarcoma. Occasionally there is a rosette like arrangement. The cells are believed to be medullo-blasts or "indifferent cells," the primitive bipotential cells derived from the medullary epithelium.

## TUMOUR OF THE ACOUSTIC NERVE

This tumour differs both in its nature and in its effects from either of the groups of intracranial tumours already considered. It arises from the acoustic nerve, from either its cochlear or vestibular fibres, and is a neurinoma derived from the neurilemma sheath (*see p. 314*). Not infrequently there are bilateral tumours. In rare cases one of the various forms of neurofibromatosis coexists.

The tumour is of slow growth, benign and encapsuled, dangerous only from its close proximity to important structures. The tumour arises usually in that part of the acoustic nerve which lies immediately outside the main cranial cavity, in the internal acoustic meatus. It forms a fibrous, grey or greyish yellow mass, firm and solid at first, though later with small areas of degeneration at the centre. The nerve fibres do not traverse the tumour, neither are they spread over its surface, but are completely engulfed and lost. The tumour slowly dilates the internal acoustic meatus and protrudes into the cranial cavity so that it lies in the angle between the pons and the cerebellum, forming a more or less oval mass which may attain a long diameter of 3 to 5 cms. As the tumour arises deep to the point at which the nerve pierces the dura, it

is invested in a capsule of meninges. In its expansion it encroaches upon the major branches of the basilar artery, which becomes incorporated in the capsule. Haemorrhage from one of these vessels constitutes a formidable risk in operation. Situated as it is in the confined subtentorial cavity, the tumour, even when small, causes much damage by impinging on adjacent structures. Neighbouring nerves are stretched and paralysed, the cerebellum is affected, and, most important of all, the pons is dislocated far from its central position, compressing and obstructing the cerebral aqueduct and leading to hydrocephalus.

Microscopically, the tumour is composed of interspersed zones of dense and of lax connective tissue. In the dense areas elongated or spindle-shaped cells are buried in a dense interlacing fibrous stroma. The cells are for the most part scanty and scattered diffusely, but they may be numerous and arranged in whorls. The nuclei usually present a palisade arrangement. Interspersed irregularly in small patches are areas of lax connective tissue with a loose reticular and almost myxomatous appearance.



FIG. 128. Acoustic neuroma.  $\times 275$ . The tumour is composed of leashes of spindle-shaped cells resembling the cells of the neurolemma sheath.

The effects of the tumour are characteristic, and are clearly reflected in a striking chain of clinical

features. For a long time the only effect is interruption of the fibres of the two divisions of the acoustic nerve, and either the cochlear or the vestibular division may be affected first. There is therefore a history that for a period of years there has been progressive unilateral deafness, often with tinnitus and some giddiness.

As the tumour expands the internal acoustic meatus, and begins to encroach upon the cranial cavity, it may cause pain, of a dull, aching character in the suboccipital region and below the ear.

With further increase in size the tumour affects other cranial nerves, which become stretched out by the dislocation of the mid-brain towards the opposite side. The trigeminal nerve is usually the earliest to be affected and there may be numbness or a sensation of burning in the field of its distribution. Involvement of the facial nerve may later lead to some degree of facial paresis. The abducent nerve, though close to the site of the tumour, escapes damage at first on



account of its length, which allows a certain degree of stretching. Later, however, its involvement leads to diplopia and strabismus.

Further enlargement leads to pressure upon the cerebellum, with ataxia and nystagmus. Most important of all, even a small tumour of the acoustic nerve may dislocate the mid brain sufficiently to cause obstruction of the cerebral aqueduct, and may form a "pressure cone" by forcing the brain stem into the foramen magnum, and with the onset of internal hydrocephalus there arise all the signs of increased intracranial pressure. The nystagmus is increased, vomiting of the cerebral type occurs, and there is an extreme degree of papilloedema.

### UNCOMMON INTRACRANIAL TUMOURS

**Angioma.** An angioma in the brain is situated most commonly in the cerebellum. It is a congenital tumour and may be associated with angiomas in other parts of the body or with other congenital malformations, and it may have a familial incidence.

Cushing and Bailey divide angioma of the brain into two major groups, the angiomatous malformations and the true neoplasms or angio-blastomata.

(1) Angiomatous malformations are developmental in origin and are sometimes associated with congenital naevi of the scalp. They may be venous or arterial in character, rarely capillary. The dilated vessels are situated on the surface of the brain generally over one cerebral hemisphere. There may be a simple enlargement of a single vessel, a tangled varicosity of several vessels, or a complicated racemose dilatation extending widely over the surface and



FIG 129 Ependymal glioma.  $\times 275$ . The tumour is derived from neuroglia cells and reproduces the primitive structure of the ependymal lining membrane of the ventricles. Some of the cells are arranged in palisade fashion round a semicircular space. Near the left margin is a pseudo-rosette.

also deeply into the substance of the brain.

Such malformations may give rise to attacks of Jacksonian epilepsy, to unilateral exophthalmos and to increased intracranial tension with papilloedema. An arterial angioma, or a venous one that has acquired secondary communication with the arterial system, may give rise to a bruit which though not so loud as that caused by an arteriovenous aneurysm, may yet be distinctly audible with a stethoscope.

(2) The angio-blastoma is a true tumour composed of cells of angioblastic origin. It is situated almost always in the cerebellum, generally near the midline close to the posterior end of the fourth ventricle. It may be solid or cystic. Three types are recognizable on microscopic examination, according as the structure is mainly capillary, mainly cellular or mainly cavernous. In its clinical course, it resembles closely and is mistaken sometimes for simple glioma.

**Dermoid Cyst.** A dermoid cyst inside the cranium is rare. It may arise either in the brain, especially in the cerebellum, or in the subdural or epidural space and may grow slowly and eventually attain large size. Occasionally an extradural dermoid cyst communicates through a small aperture in the bone with a cyst in the soft tissues of the scalp or face, especially at the external orbital margin.

**Tumours of the Pineal Gland.** These are of the nature of gliomata or teratoma. Both varieties affect young adults, usually of the male sex. They do not grow rapidly, but from their situation may tend even when small to obstruct the cerebral aqueduct and to lead to hydrocephalus. The first and often the only one, may be that of increased intracranial tension. Sometimes, and especially in the case of a teratoma, there is some degree of sexual precocity, which is believed to be due to an increased functional activity of the gland.

**Tumours of the Ependyma.** The ependyma, the lining membrane of the ventricles, is derived from spongioblasts, which early in their histogenesis become differentiated from the cells destined to form the neuroglia. Ependymal cells are characterized by the possession of cilia and tiny, rod-like, deep extensions of their protoplasm—blepharoplasts. Both these characteristics may be reproduced in the tumours. Ependymal tumours occur usually in relation to the fourth ventricle. They are of slow growth but lead rapidly to obstructive hydrocephalus. They may be found, rarely, in other parts of the ventricular system.

**Sarcoma.** It seems probable that a true primary sarcoma in the brain is of extreme rarity, and that the majority of tumours previously regarded as of that nature are gliomata. A true malignant mesoblastic tumour may arise from the perivascular connective tissue. Occasionally a sarcoma at some other part of the body may metastasize to the brain.

**Tuberculoma.** This is a tuberculous mass, either a solitary follicle or, more commonly, several confluent nodules. It occurs most often in children, and usually affects the cerebellum or the frontal lobe, and forms a lump which at first is firm and rounded, but later caseates. It may attain the size of an egg, and, especially when situated in the cerebellum, gives rise to clinical features which may simulate those of a tumour. It commonly leads to a fatal issue by infecting the meninges. In rare instances it becomes totally calcified.

**Gumma.** A gumma originates in, or close to, the meninges as single or multiple nodules. The nodules are grey or greyish red, and, in their progress, they resemble gummata elsewhere. They tend to undergo central softening and, later, to heal with the production of much scar tissue and with serious cerebral impairment.

## EFFECTS OF INTRACRANIAL TUMOURS

The symptoms of intracranial tumours fall naturally into two groups—those due to the local effects of the tumour upon the adjacent brain and membranes and those which result from an increase of intracranial tension.

Those of the first group are the focal symptoms which vary with the situation and character of the individual tumour. Their consideration would include the whole subject of topographical diagnosis which is outside the scope of the present work.

The second group includes the classical triad, headache, vomiting and papilloedema (optic neuritis), and also giddiness, convulsions, changes in mentality, and the signs characteristic of hypopituitarism.

*Headache* may be due either to localized pressure of the tumour or to a general increase in the intracranial tension. Local pressure pain is most characteristic of meningioma or it may occur when an acoustic nerve tumour expands the auditory meatus. The pain is usually localized to one side of the head or even to a particular spot, and, in the case of a meningioma, there may be tenderness on pressure. Subtentorial tumours sometimes give rise to pain referred to the nape of the neck. Headache from increased intracranial tension is most severe with tumours that lead to internal hydrocephalus, such as tumours of the acoustic nerve, the cerebellum and the fourth ventricle. The pain is paroxysmal, worst at night and in the early morning and is precipitated by any action such as coughing, straining or pressure upon the veins of the neck, which will lead to an increased tension inside the skull. Cerebral oedema is probably an important cause of headache.

*Vomiting* like headache, is most frequent at night and in the early morning. It is probably due to increased intraventricular pressure, which affects the vomiting centre of the medulla. It is most frequent when internal hydrocephalus is present.

*Papilloedema* (optic neuritis) is a state of venous congestion of the optic disc and retina. It is due, in all probability, to compression of the central vein of the retina as it leaves the optic nerve and passes across the subarachnoid space of the optic sheath. It is most obvious with tumours of the temporal lobe, the cerebellum and the fourth ventricle and may be absent in subcortical cerebral tumours. The optic cup of the retina, normally depressed below the surface, fills up with oedema and may even project above the general retinal surface. The oedema spreads to the retina around it, the veins become greatly engorged, hæmorrhages may occur and eventually secondary optic atrophy develops. Vision may remain unimpaired for a long time but eventually there may be total blindness.

*Giddiness* may be a symptom of general increase in pressure or it may result from a direct effect of a tumour upon the apparatus of equilibration. It is seen most often with tumours of the acoustic nerve, the cerebellum and the pons.

*Hypopituitarism* is a secondary effect of an increase of intracranial pressure, and is especially common when the tumour has given rise to

a state of internal hydrocephalus. The floor of the third ventricle dilates, exerts pressure upon the base of the skull, and leads to erosion of the clinoid processes and flattening of the pituitary fossa. Either from direct pressure upon the gland itself, or from obstruction to the flow of its secretion into the cerebrospinal fluid, there results a condition of hypopituitarism, with obesity, polyuria, increased sugar tolerance and sexual infantilism. The effect of intracranial tumours upon the pituitary may be demonstrated in radiograms, for erosion of the clinoid processes and enlargement of the pituitary fossa are well recognized radiographic signs of increased intracranial tension.

*Affections of the cranial nerves* may result from hydrocephalus. They are believed to be due to stretching of the nerves from downward displacement of the brain. The abducent nerve is involved most commonly, occasionally the trigeminal and rarely the oculomotor and facial. It is important to recognize that these disturbances are merely evidence of intracranial hypertension. They are of no value in the localization of the tumour.

## DISEASES OF THE PITUITARY GLAND

It is no cause of wonder that so small an organ as the pituitary gland should play so important a part in the growth of the body and its metabolism. The gland is connected by the infundibulum to the tuber cinereum of the floor of the third ventricle. It is little larger than a pea, yet it exercises, through its internal secretions, a profound influence on growth, sexual functions, metabolism, etc.

It consists of four parts—*anterior, intermediate, tuberal, and nervous*—which differ from one another in derivation, in structure, and probably in function. The *pars anterior* is usually spoken of as the anterior lobe, and the *pars intermedia* and *pars nervosa* together as the posterior lobe. Between the two lobes there is a cleft like space which contains glial fluid. The *pars anterior* and the *pars intermedia* are ectodermal in origin, and arise from a tubular protrusion of the oral epithelium. The *pars nervosa* also is of ectodermal origin, but is derived from the neural ectoderm, and arises as a downgrowth from the floor of the third ventricle. The *pars tuberalis* is formed from a separate outgrowth of the oral ectoderm, and in some animals it remains separate from the rest of the gland.

### Histological Structure of the Pituitary Gland

The *pars anterior* is composed of two distinct kinds of cells—clear and granular. The clear cells are known as chromophobe cells, and the granular as chromophil cells. There are two types of granular cells—basophil and eosinophil, both are derived from chromophobe (mother) cells and by special staining methods transitional types of each can be recognized. Normally the chromophobes constitute 52% the eosinophil 37% and the basophil 11% of the cells in the *pars anterior*. The basophil cells are increased in number following castration and after thyroidectomy.

The *pars intermedia* (poorly developed in man) is a thin strip of

tissue composed of clear non granular cells, amongst which there are vesicles filled with colloid. In places its cells extend into the pars nervosa and undergo degeneration to form hyaline or granular colloid material. These "colloid bodies" pass upwards through the pars nervosa and are eventually set free in the cerebrospinal fluid of the third ventricle. The colloid is therefore regarded as the active secretion of the pars intermedia and is probably derived from the basophil cells of the anterior lobe. Its production is greatly increased after thyroidectomy.

The pars nervosa is composed of neuroglia and ependymal cells. It contains no cells of a definitely neuronic character. Developmentally and functionally the posterior lobe participates in the complicated processes attributed to the hypothalamus, from which it is an outgrowth.

The pars tuberalis is different in structure from the rest of the gland. It surrounds the infundibulum and forms a sheath for it, and at the base of the brain spreads over the tuber cinereum. The pars tuberalis is exceedingly vascular and looks not unlike thyroid tissue. It contains areas of squamous epithelium formed, it is believed, by a process of metaplasia. In lower vertebrates this part of the gland controls melanophore activity.

### The Functions of the Pituitary Gland

Knowledge of the functions of the pituitary gland though still incomplete has been greatly enhanced by clinical pathological and experimental observations and it is now proved that the gland occupies a dominating position in the endocrine system governing directly or indirectly a surprising number of biological processes.

The anterior lobe provides at least six or more hormones. They are (1) *gonadotropic* which controls the development of the sex glands and the various phases of the reproductive cycle. The large quantities of the hormone found from an early stage of pregnancy in the urine and blood are the basis of the Aschheim Zondek biological test for pregnancy. (2) *Growth* which controls skeletal development and the time of fusion of epiphyses. (3) *Thyrotropic* suggested by the experimental observations that hypophysectomy causes thyroid atrophy whose effects can be controlled by replacement therapy. Excessive dosage of extracts of the pituitary leads to hyperplasia of the thyroid and a condition resembling toxic goitre. (4) *Adrenotropic* which controls the size and activity of the suprarenal cortex. (5) *Lactogenic* which promotes lactation at the end of pregnancy, and is believed to confer the mother instinct in animals. (6) *Diabetogenic and ketogenic* suggested by the observations that (a) diabetes disappears from a depancreatized animal after hypophysectomy, and (b) that injections of anterior lobe extract will produce diabetes and ketonuria.

The posterior lobe may be removed without fatal result, and indeed without demonstrable effect. Very little is known of its normal physiological action, but it is believed to participate in the important metabolic functions subserved by the hypothalamic nuclei. The extract of the posterior lobe (*pituitrin*) has very active pharmacological and hormonal effects, but its mode of action in normal conditions is not yet determined.

The extract contains two easily separable active principles—*pitressin* and *oxytocin*. Pitressin raises blood pressure, stimulates peristalsis, antagonizes insulin and suppresses the diuresis which follows a large intake of fluid. Oxytocin is a powerful stimulant of plain muscle and terminates pregnancy, and in this property antagonizes the hormone of the basophil cells of the anterior lobe of the pituitary.

### Manifestations of Disorders of the Pituitary Gland

In the light of the known and suspected functions of the pituitary, the origin and features of its diseases are easily understandable, and it is obvious that not the pituitary entirely but other endocrine glands especially the sex glands, share in producing the familiar clinical syndromes.

(1) *Pituitary Deficiency (Aplutuitarism and Hypopituitarism)* The manifestations of deficiency vary according to the extent to which activity of the gland is suppressed and the age of onset. The anterior lobe may be destroyed in whole or in part by septic embolism, venous infarction, syphilis, cysts, etc. Considerable interest is attached to necrosis of the anterior lobe. It has been encountered most often as a complication of parturition in which there has been severe hemorrhage. Destruction of the gland is confined to the anterior lobe and may be patchy or widespread. The cause appears to be thrombosis of the veins and sinusoidal vessels of the gland with resulting necrosis.

If the disease is survived there may be pituitary deficiency of any degree with features varying according to the age of the subject. In most cases the uterus involutes, lactation ceases and there is grave asthenia. The severer grades of the disease associated with cachexia and premature senility are described under the title of *Simmonds' disease*. It is of interest to note that in a few instances on the occurrence of another pregnancy the pituitary deficiency has disappeared doubtless from the result of stimulation of the remaining tissue of the gland.

Less severe grades of deficiency are much more common. They may be due to delayed development of the gland, hydrocephalus, or the destructive effects of tumours. In children the most striking changes are infantilism and adiposity. With infantilism the body is not necessarily short but is slender. The sexual organs are immature, secondary sexual characteristics fail to develop, and puberty does not occur. Obesity may be generalized, or may be localized to the pubic area (*dystrophia adiposa genitalis*). Anaemia of microcytic or macrocytic type may be a conspicuous feature.

In young adults the most notable changes are depression of the sex function and obesity with increase of carbohydrate tolerance. In men there are depression of sexual activity and genital atrophy. In women, amenorrhoea is often an early manifestation, and later the genital organs involute.

(2) *Pituitary Over-activity (Hyperpituitarism)* Pituitary over activity is most commonly due to excessive secretion of the eosinophil cells (hyperpituitarism) and much less frequently to exaggerated activity of the basophil (basophilism). There is a syndrome characteristic

of each. The latter is often associated with pathological changes in the suprarenal cortex.

(a) When hyperpituitarism develops during the period of growth, gigantism occurs, in later life acromegaly.

In gigantism growth of the skeleton continues beyond the usual period of adolescence, and the epiphyses remain ununited. In addition, the sex organs often remain atrophic, and the secondary sexual characters are under-developed.

In acromegaly the most obvious changes are overgrowth of the skeleton, most definite in the skull and facial bones, and in the vertebral column and phalanges. The chief changes in the skull are increased thickness of the bones and enlargement of the natural ridges. In the face the zygomatic bones become prominent, the mandible enlarges (prognathism), and as the teeth do not enlarge coincidentally with the jaw they may be widely separated. Kyphosis in the thoracic region is the most notable change in the vertebral column. The phalanges are enlarged and exostoses may develop on them.

In prolonged hyperactivity the skin and subcutaneous tissues become thick, inelastic, and coarse. Other soft organs may be enlarged: the nose is broad, the lips thick, and the tongue hypertrophied. Internal organs also, e.g. the colon, may be enlarged.

(b) In over activity of the basophil cells arising from an adenoma, a very characteristic syndrome may develop—the pituitary basophilism of Cushing. The features of this condition resemble closely those of a tumour of the adrenal cortex (see p. 606), and it may be difficult to ascertain whether pituitary or adrenal gland is responsible.

However, it has been shown by both biological and colorimetric assays of the urine that, especially in females, the androgen output per day in the case of adrenal cortical tumours is as high as 250–300 international units (normal 16 to 80 units) whereas in Cushing's syndrome the androgen output lies within the usual limits or is slightly lower than normal.

It affects women much more frequently than men. The onset is fairly abrupt with a marked increase of the subcutaneous fat of the face, neck and trunk. The skin assumes a dusky or plethoric appearance, and purple lineæ atrophicæ may develop. Hirsuties is a striking feature. The patient suffers from headache and abdominal pains and is easily fatigued. In women amenorrhœa occurs early, in men impotence. There is commonly pronounced decalcification of the skeleton which may lead to kyphosis, and in many instances, to fractures of the long bones. A very constant feature is vascular hypertension and a tendency to polycythæmia. The urine may contain a follicle stimulating substance. At post mortem, hypertrophy of the ovaries, the thyroid gland and the suprarenal cortex is commonly present.

(3) Additional Signs of Disease of the Hypophysis (a) *Diabetes insipidus* is an inconstant feature, it sometimes results from the pressure of suprasellar tumours. It is now conceded that the extreme polyuria, excessive thirst and emaciation are due to involvement of the hypothalamic nuclei which control water metabolism. The pituitary may be destroyed or removed without the occurrence of diabetes

insipidus, yet even if the pituitary is not implicated, injections of pituitrin are usually effective in controlling the polyuria. Thyroidectomy may benefit intractable cases.

(b) *Adiposity*, though often a very striking feature, is an inconstant one. It is much commoner in young subjects. It is probable that the adiposity is secondary to atrophy of the sex glands and therefore resembles the obesity that may follow castration.

## TUMOURS OF THE PITUITARY GLAND

Tumours are the commonest diseases of the pituitary gland and account for about 15% of all intracranial tumours. They are classified according to the tissue from which they arise, and according to their position relative to the gland itself. A simple adenoma is by far the commonest. It arises in the anterior lobe, and while small is entirely within the sella turcica—i.e., intrasellar. It is named chromophobe, chromophil, basophil, or transitional, according to the pattern of cell which predominates. An adenocarcinoma may occur but is exceedingly rare. The other common tumours arise in relation to the pars tuberalis and are of epidermoid character (cranio-pharyngioma) and, in exceptional cases, from the interglandular cleft in the form of a distension cyst of an embryonic vestige (Rathke's embryonic invagination of the stomodeum). The epidermoid tumours from their anatomical position and their common (though not invariable) cystic character, are known as *suprasellar cysts*.

Primary tumours in the pars nervosa are unknown, but it is frequently the seat of metastases.

### Pituitary Adenoma

The adenoma is a small tumour, usually of pale yellow colour, but may become a dark maroon from extravasated blood. It is soft or firm, according to the rate of growth and, like other adenomata, may become cystic.

The chromophobe adenoma is much the commonest type and occurs between the ages of twenty and forty years. It is composed of groups of clear, non granular cells of an embryonic type (see Fig 130), they may be arranged in alveoli,



FIG 130 Chromophobe adenoma of the hypophysis. The cells are large, non granular, and uniform in shape and size.



flat sheets, or in papillary formation. The tumour furnishes no endocrine secretion, and its pathological effects are due to the pressure it exerts on the hypophysis. The constitutional effect of

such a tumour is therefore hypopituitarism, in which there may be inhibition of both growth and maturation.

The chromophil or eosinophilic adenoma is usually of smaller size and is composed of richly granular cells that resemble the normal epithelium of the anterior lobe (see Fig 131). Chromophobe cells also are almost always present but they are not of an embryonic type. The tumour, although it impinges upon and destroys the hypophysis, produces an endocrine secretion,

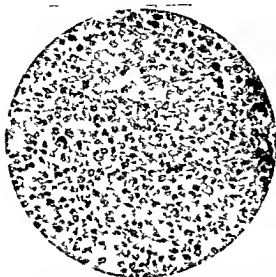


FIG 131 Chromophil adenoma of the hypophysis from a case of acromegaly. The sinusoidal character of the normal anterior lobe is lost. The cells are large and irregular and the majority are acidophil.

and it is constantly associated with the syndrome hyperpituitarism, usually evidenced by marked sex dysfunction. As it is most common after the age of twenty years, acromegaly is the usual result.

The transitional or mixed adenoma is composed of chromophobe cells with eosinophilic cells in varying numbers. It is usually larger than a pure eosinophilic adenoma. It destroys the gland but on account of its content of eosinophil cells it maintains the secretion, with the result that there may be blending of the features of hypo- and hyperpituitarism. The common age of occurrence is twenty to forty years.

The basophil adenoma is the rarest type of pituitary tumour. It is usually small, seldom more than 2 cm in its greatest diameter, and therefore pressure effects are lacking. Microscopically, it resembles an eosinophil adenoma, but with special stains the cells are found to contain basophil granules. The tumour may be associated with Cushing's syndrome or "basophilism" (see p 606) but the relationship is not constant, and sometimes a basophil adenoma causes no symptoms. When present it has been observed that the basophil cells of the gland show degranulation of their cytoplasm but the cells of the tumour are unaltered. There is evidence that primary degenerative changes in the hypothalamus may be followed by hyalination of the

cells of the pituitary and the features of Cushing's syndrome.

It is exceedingly rare. It is composed of cells

of chromophobe type arranged in irregular groups or solid cords, it is very vascular, and cystic degeneration frequently occurs in it. The tumour destroys the hypophysis, invades the cranial bones and nerves, and causes paralysis. Metastases may occur in the liver and elsewhere. Most cases have occurred after the age of forty-five years.

**Cysts of the Interglandular Cleft (or Rathke's Pouch)** In rare instances a cyst may develop in connexion with the epithelial lining

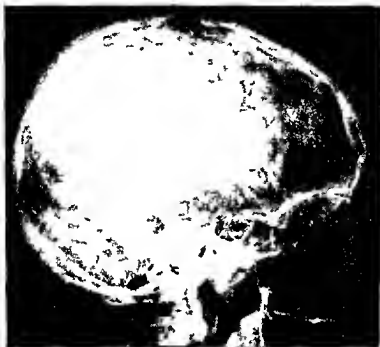


FIG 132 Pituitary adenoma. Note the expansion of the sella turcica  
(By courtesy of Dr Scott Park)

of the interglandular cleft. It is lined with a single layer of columnar epithelium which may be ciliated. The cyst is intraglandular and intrasellar in origin and therefore destroys the gland and by extension may produce local pressure effects.

#### The Local Effects of Adenoma of the Pituitary

Growth of an adenoma is much restricted by the bony boundaries of the sella turcica and its dural roof—the diaphragma sellæ. It is therefore not surprising that the gland is gradually compressed and destroyed by the expanding tumour. In its attempt to secure accommodation the tumour expands the bony walls of the sella turcica which in a radiogram shows a characteristic globular distension (see Fig 132). Finally, the bone may be eroded so that the tumour projects into the sphenoidal air sinus and may lead to epistaxis and pharyngeal discharge. Lateral expansion of the tumour compresses or displaces the cavernous venous sinus and may paralyse the oculomotor or the abducent nerve, occasionally the ophthalmic and maxillary divisions

of the trigeminal nerve are affected. Upward extension causes stretching and occasionally rupture of the diaphragma sellæ, and when that happens the tumour may impinge on the optic chiasma. As a rule it is the antero-inferior part of the chiasma that is subjected to pressure, and primary optic atrophy with blindness occurs. The characteristic change in the visual field is bitemporal hemianopia manifest first in its upper lateral quadrant. At a later stage the hypothalamic region and the uncinate area of the hippocampal gyrus may be indented by upward and lateral extension of the tumour, and somnolence and other effects referable to pressure on these structures are produced. Only when the third ventricle is compressed or the aqueduct obstructed do signs of increased intracranial tension become evident.

### Suprasellar Epidermoid Tumours (Cranio-pharyngioma)

The common suprasellar tumour is of epidermoid character. It is commonest in youth and over 75% occur before the age of forty years. The tumour arises above the diaphragma sellæ in relation to the pars tuberalis from islets of squamous cells within that structure. Whether the cells are embryonic rests or developed by metaplasia has not been fully settled.

The tumour is usually cystic but may be solid. At the base of the cyst there is generally a warty projection. Histologically, it is of epidermoid structure, most often well differentiated with keratinization and cell rests, sometimes of basal cell type, and rarely of enamel cell type (adamantinoma). Fatty substances are frequently present in the stroma and their calcification (which is present in 85%), affords a significant sign in radiographic interpretation.

A suprasellar tumour usually begins just beneath the aperture of the diaphragma sellæ, and, at this point, lies within the cisterna chiasmatis. As growth proceeds it bulges upwards rather than downwards, on an average it has the dimensions of a walnut but may be very much larger.

A suprasellar cyst has no endocrine secretory faculty and its effects are referable chiefly to pressure. At an early stage it impinges on the hypothalamus, and therefore polyuria is an early symptom. Later there may be compression of the optic chiasma and the pituitary, and the combined effects may result in Frohlich's syndrome and diabetes insipidus. The dorsum sellæ and the clinoid processes may be eroded as a result of pressure and, in a radiogram, such changes may afford valuable evidence in diagnosis.

### Surgical Aspects of Pituitary Tumours

Suprasellar tumours bulge into the subarachnoid space and impinge on the mid brain, the optic nerves or chiasma. The tumour may be very firmly adherent to the margins of the sella turcica. Removal of a suprasellar tumour is only possible by an intracranial operation, and when it is situated laterally or far back access may only be obtained by sacrifice of one of the optic nerves. In operating care must be exercised to avoid laceration of the floor of the third ventricle, an accident which usually proves fatal.

In pituitary adenoma operation is designed to relieve headache and to prevent or relieve blindness. In a few cases progression of endocrine disturbances may be prevented. For preference, the tumour is approached from within the skull and an attempt is made to remove the greater part of it. When an adenoma is of slow growth and has not developed an intracranial extension, and especially, as in acromegaly, when the subject is in poor condition, it is most easily dealt with by the transphenoidal route, which permits of a partial removal of the tumour and affords a decompression of the expanded sella turcica. In rare instances tumours bulge into the third ventricle and are only accessible via the frontal lobe and lateral ventricle.

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## CHAPTER XIV

### DISEASES OF THE SPINE AND SPINAL CORD

#### SPINA BIFIDA (*Rachischisis*)

THE spinal cord, like the brain, is derived from the ectoderm of the dorsal surface of the embryo. A strip of ectoderm, the *neural plate*, becomes raised above the general surface, and then in succession hollowed out as a groove, depressed below the surface, and folded sagittally to form a tube. This *neural tube* later becomes further depressed, and then separated from the surface ectoderm by an intrusion of mesoderm growing in from either side. The processes of tubulation and of separation from the skin surface are completed last in the lumbar region, and it is here that developmental anomalies are most common.

There are many types of spina bifida, but some of these being incompatible with life are of interest only to the teratologist, and for practical purposes a simple classification will suffice.

(1) **Complete Rachischisis.** This is a gross abnormality resulting from failure of development of the whole length of the column. The cord fails entirely to separate from the superficial ectoderm and remains exposed to the surface in a shallow gutter in the midline of the back. The condition is incompatible with life.

(2) **Partial Rachischisis.** This type includes all the less extensive defects that involve only a limited portion of the cord. The defect is most often situated in the thoraco-lumbar or lumbo-sacral region, rarely in the cervical region. It may be a severe lesion, incompatible with life, or may be so small as only to be discovered on careful examination. Three principal varieties and two rare ones are recognized.

(a) **Myelomeningocele.** This is a gross deformity, and often the child is still born or dies within a few days of birth. There is a defect of the vertebral laminae and spines and in the soft tissues over a limited area, usually in the thoraco-lumbar region, and the cord in this part of its course lies in its primitive position close to the skin surface. Three or more of the vertebrae are usually affected. The spinous processes are absent, the laminae are represented merely by short stump like projections, and the vertebral canal consequently forms a shallow trough with no posterior wall. The cord, which at higher levels lies normally in the vertebral canal, at the position of the defect comes to lie more superficially. In some cases it lies completely exposed in the floor of a shallow gutter, and it then has a raw red appearance as of congested granulation tissue. This variety is sometimes known as a *myelocele*.

In other cases the cord is raised on the surface of a cystic swelling, which is sometimes of large size. Since this is the type most often seen surgically it requires a fuller description. The protrusion is situated

in the midline, where it forms a somewhat oval and irregularly lobulated sessile mass, in the summit of which lies the abnormally placed cord. The cord, retaining the shape of the embryonic neural plate, forms a flat, plaque-like strip of tissue which is evident as an oval area, bluish or congested—the *area medullo-vasculosa*. In some cases this area is covered with a thin layer of epidermis, with which it is closely fused. In other areas, epidermis is lacking, and the nerve tissue is covered only by soft red granulations. Near the upper end of this area there is sometimes a small orifice, which represents the termination of the central canal of the cord. For the first few days of life a little cerebrospinal fluid may escape here, but the orifice is soon closed by œdema. Occasionally a similar orifice is present at the caudal end.

Around the *area medullo-vasculosa* and continuous with it lies the *zona epithelio-serosa*, which represents the area of fusion of the skin

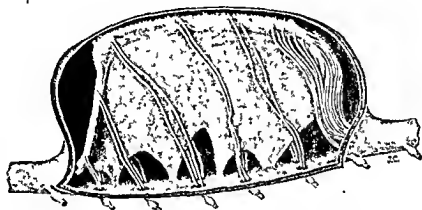


FIG. 133. Myelomeningocele exposed by longitudinal section. The malformed spinal cord is seen at the summit of the sac. On the right, the filaments of the cauda equina pass deeply to gain the vertebral canal. Note the expanded ligamentum denticulatum.

(By courtesy of Professor Sir J. Frazer.)

with the membranes lining the sac, the dura mater and arachnoid. It is thin and often of bluish colour, and laterally, where it gradually merges with the surrounding skin, there are often small telangiectases and epithelial overgrowths.

The sac may be unilocular or multilocular. It contains cerebrospinal fluid, and on its deep aspect it communicates with the spinal subarachnoid space, of which it is merely a greatly enlarged portion. The cavity is traversed by pairs of nerve roots, which arise in the abnormally placed portion of the cord and proceed deeply to the vertebral canal to gain exit through the intervertebral foramina. Each nerve, as it traverses the sac, is supported by a fold of arachnoid, which attaches it, as by a mesentery, to the sac wall. The sac is also partly divided into compartments by the ligamenta denticulata, which form broad sheets that pass backwards on either side of the midline. Sometimes at the lower end of the sac the cord is reconstituted and re-enters the spinal canal. More often, however, the termination of the cord lies in the sac

and the fibres of the cauda equina pass deeply to gain the canal and their proper exits

A myelomeningocele is often accompanied by other defects. There are usually deformities of the lower limbs or paralyses resulting from failure in the development of the cord and there may be such unrelated lesions as hypospadias, cleft palate or hare lip. Hydrocephalus is often present. The treatment is very unsatisfactory, for though it is technically possible to replace the cord in its proper position this does not rectify the associated paralysis. Moreover, the operation itself is a severe one for a young infant and since the surface of the exposed cord cannot be sterilized, meningitis often supervenes.

(b) *Meningocele* This is a rather uncommon deformity. It may be likened to a herniation of the meninges of the cord (arachnoid and dura mater) through a gap in the bones and soft parts. The cord itself is unaffected and lies in its bony canal and the nerve roots usually lie

in their normal position. The spinous processes of the affected vertebrae usually two or three in number, are absent, and the laminae are represented merely by short projections on the posterior surfaces of the transverse processes.

The membranes projecting through this gap form a cyst like swelling under the skin in the midline of the back. Typically, the swelling is covered by thin skin which may be scarred in places. It contains cere-



FIG. 134. Cervical meningocele.

brospinal fluid and is translucent. Usually there is no associated paralytic lesion but hydrocephalus or other congenital deformities may be present.

(c) *Spina Bifida Occulta* Here the obvious defect is minimal. The cord is completely formed and lies in its bony canal and the membranes are intact but the spines and laminae of one or more vertebrae are abnormal. Sometimes the spines are absent and the laminae defective and there is a palpable defect in the midline of the back. In other cases the spines are bifid. The skin surface may be of normal appearance but often is dimpled and there may be dilated vessels, a tuft of hair or small fatty or fibrous tumours.

The defect may give rise to no symptoms and remain unrecognized except perhaps on chance clinical or radiographic examination or it may lead to paralytic deformities of the lower limbs such as pes cavus or other forms of talipes. These deformities usually develop during adolescence and are often bilateral.

The paralytic effects are attributable to the presence of the *membrana reunens*, a tough fibrous band passing from the deep aspect of the

skin to the membranes of the cord. In early life the *membrana reunens* remains lax and causes no symptoms, but during adolescence or early adult life it fails to keep pace with the growth of the rest of the body and with the slight upward movement of the cord in its canal, so that traction may be imposed upon it. The dura mater, to which the membrane is attached, is drawn superficially and slings the cord in that direction. Thus the pull of the *membrana reunens* is transmitted to the anterior part of the cord, which is compressed, and consequently the paralytic phenomena are almost entirely motor. Trophic changes in the skin, especially of the feet, are common.

(d) *Syringocoele* (*Syringo myelocoele*) In this rare anomaly the cyst like swelling represents a greatly dilated portion of the central canal of the cord, and the cavity is consequently lined by modified compressed nervous tissue.

(e) *Anterior Rachischisis* This is an exceedingly rare form of rachischisis in which the sac protrudes anteriorly, through a defect in the vertebral bodies. It may form a protrusion in the abdomen or pelvis and be mistaken for a tumour or cyst. It is rarely compatible with life and is not amenable to treatment.

### SPONDYLITIS DEFORMANS

This title includes a variety of diseases of the spinal column characterized by varying degrees of stiffness and pains in the back. In some cases the disease affects young adults, causing much pain and progressing to complete rigidity of the back with marked disability, in others it affects elderly persons, giving rise to the rounded shoulders, bent back and stiffness so common in old age.

Sometimes a cause is to be found e.g., a dental focus of infection or a gonococcal prostatitis, more often the origin of the disease can only be ascribed to chronic degenerative changes or to repeated trauma.



FIG. 13. Spondylitis deformans. The vertebral column is ankylosed in a position of kyphosis. There are osteoarthritic changes in the intervertebral and costo-vertebral joints and the vertebral bodies are united by plaques of new bone.

(Museum of Royal College of Surgeons of Edinburgh)



Two main types may be recognized the osteo arthritic and the ankylosing types

**Osteo-arthritis of the Spine** This disease may occur alone or in association with disease of other joints, and it is generally regarded merely as a special type of osteo-arthritis with certain special features related to the special anatomy of the spine. The disease commonly occurs in elderly people. The articulations are affected primarily, later the ligaments and the intervertebral fibro-cartilages may be involved. In some cases the disease affects multiple intervertebral joints and also the costo-vertebral joints, in others, and more commonly it is localized to one part of the column, particularly the lumbar segment. The articular cartilages and bone are eroded and chondro-osteophytes develop at the margins. Often also exostoses arise from contiguous margins of the vertebral bodies and project laterally as sharp spurs, or bridge the gaps between adjacent bodies. The intervertebral fibro-cartilages undergo gradual absorption and become thinned, as though from pressure, while not infrequently the vertebral bodies become wedge shaped. Very rarely the ligaments of the vertebral column become ossified.

Arthritis of the spine causes stiffness of the back and may cause "rheumatic" pains, which are accentuated by climatic changes or by sudden twisting movements. Often the pain is referred to the distribution of sensory nerves, particularly the sciatic nerve. These effects are usually ascribed to pressure of osteophytes on the nerves as they emerge from the intervertebral foramina, hence the special tendency to involvement of the fourth and fifth lumbar roots of the sciatic, which are large nerves almost filling the bony canals.

**Spondylitis Ankylopoietica** This very disabling disease generally occurs in young adults, especially in males, and gives rise to severe persistent pain and marked rigidity of the spinal column. It may progress rapidly until the whole spine—and the sacro iliac joints and sometimes also the hip joints—are completely ankylosed, or it may take a chronic course with remissions lasting many months or years.

The first signs are often seen in relation to the sacro iliac joints, later all the intervertebral and costo vertebral joints may be involved. The joint cartilages are eroded and the bone adjacent undergoes rarefaction, and this is later followed by osseous ankylosis, so much so that eventually in radiographs no trace of the joint outline remains. The intervertebral cartilages also are thinned, while exostoses projecting laterally bridge the gaps between contiguous vertebrae, giving a radiographic appearance often compared to a bamboo stick. The disease responds very favourably to irradiation by X rays.

## AFFECTIONS OF THE INTERVERTEBRAL DISCS

The investigations of Schmorl have focussed attention upon certain affections of the intervertebral discs which had not previously been recognized. A disc consists of three portions. There is a peripheral ring, the *annulus fibrosus*, composed of tough fibro-cartilage firmly attached to the vertebral bodies and to the anterior and posterior

longitudinal ligaments. On the two surfaces of the disc are thin plates of hyaline cartilage, which are set directly in contact with the spongy bone of the vertebral bodies. These plates serve a double function acting as epiphyseal cartilages for the vertebral bodies as well as retaining capsules for the nucleus pulposus.

The *nucleus pulposus* the third element of the intervertebral disc is contained within the annulus and between the cartilage plates. It forms a semi gelatinous mass consisting of loose fibrous tissue containing scanty cartilage cells and large multinucleated cells (rudiments of the notochord) set in a gelatinous matrix. The nucleus is confined within the disc under tension imparting an elastic quality to it, and thus giving a high degree of resilience to the vertebral column as a whole.

Prolapse of the nucleus through a defect in the enclosing shell is now recognized as an important cause of backache and sciatic pain and other pressure effects.

The cause of prolapse of a disc is not clearly established. Sometimes there is a history of an injury which usually takes the form of a fall with the spine in flexion or of a strain sustained while lifting a heavy weight. The frequency of a history of such an injury has varied greatly in different series and few observers claim that it is to be found in more than 20-25% of cases. Often moreover the injury is of a relatively slight character. Consequently it may be assumed that the injury if present only serves to determine the prolapse of an already degenerate disc.

Generally the disc is extruded posteriorly towards the spinal canal where it appears as a small glistening white swelling to one side of the posterior longitudinal ligament. Less often it appears as a diffuse bulging in the midline deep to the longitudinal ligament. In some cases a so called concealed prolapse is present which only becomes manifest when the spine is flexed.

The commonest site of prolapse is in the lumbar region particularly at the fourth and fifth lumbar spaces and the lumbosacral space. In this region the disc will press upon the roots of the sciatic nerve or rarely, the cauda equina.

The precise pressure effect depends on the level of the prolapse and its distance from the midline. A prolapse placed laterally compresses the nerve root as it traverses the intervertebral foramen whereas one placed nearer the midline will affect a root passing down the spinal canal towards a lower foramen. Thus a prolapse of the fourth disc if lateral will involve the fourth root whereas if further medial it will involve the fifth or one of the sacral roots.

In addition to root pressure (usually manifest as sciatica) the prolapse may give rise to flattening and fixity of the lumbar spine and pain low in the back. Rarely the prolapse causes partial obstruction of the thecal space and produces an increase in the protein content of the fluid obtained on lumbar puncture.

Cervical disc lesions are less common but the relative fixity of the cord in the cervical region renders it more liable to damage. Hence in addition to root pain and paræsthesia a prolapse at this level may give rise to signs of cord compression.

reason it is situated, in 75% of cases, on the postero-lateral aspect of the cord; less commonly it appears to arise from an anterior root or from the meninges in front of the cord. In the majority of cases the thoracic portion of the cord is affected, but no portion is exempt.

Usually the tumour is of firm, fibrous consistence and has a somewhat scanty blood supply derived from a single small arterial twig. In other cases the vascularity is greater. Often the tumour is partially calcified, and is then sometimes known as a *psammoma*.

Microscopically, it resembles an endothelioma. Flattened endothelial cells, or spindle-shaped cells of fibroblastic type, are set in a well-formed fibrillar stroma. Often the cells exhibit whorl-formation. There are usually areas of hyaline degeneration and of calcification, and there is often some lymphocytic infiltration.

**Effects of the Tumour.** The effects of tumours of the intradural extra-medullary group are usually characteristic. At first only the related nerve root is affected. Later the cord is displaced and compressed, though never invaded. Pressure upon the cord for a long time causes only irritation and œdema. Later the nerve cells and fibres undergo pressure necrosis (sometimes aggravated by thrombosis of vessels), and irreparable damage is done. The meninges around the tumour, though not invaded, are curiously thickened, as though inflamed, and are often unduly vascular.

The pathological changes are reflected in the clinical features. At first there is evidence of interference with a single posterior nerve root. "Root pain" is referred to the area of distribution of the nerve, and there may be paresthesiæ, with sensations of tingling, numbness, heat and cold. Complete block of nerve conduction may lead to areas of anæsthesia, but this is often masked by the overlapping distribution of adjacent sensory nerves.

At a later stage the tumour presses upon and indents the cord,

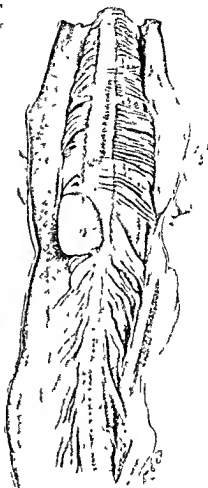


FIG. 130. Spinal meningioma. The tumour lies in close relation to the posterior nerve roots of the cervical enlargement of the cord. The tumour is of small size and encapsuled. It has compressed, but not invaded the cord.

(Department of Clinical Surgery, University of Edinburgh.)

affecting first the nearest cells and tracts, later half the cord and eventually its whole thickness. The effect of pressure is to damage the grey matter at the level of the tumour, and to interrupt impulses conveyed by the fibres in the white matter. Thus a tumour pressing on the lower cervical cord may give rise to a lower neuron paralysis of the arm on the corresponding side, and an upper neuron paralysis of the lower parts of the body. When only half the cord is affected the Brown-Séquard syndrome may result, in which there is muscular paralysis with loss of deep sensation on one side and paralysis of the sensations of pain, heat and touch on the other. Eventually the tumour compresses the entire cord and complete paraplegia develops.

When the tumour grows sufficiently to press upon and stretch the surrounding membranes, it may give rise to pain locally over the affected portion of the spine, and this area becomes tender on direct pressure.

In those regions where the cord occupies most of the available space, as at the cervical and lumbar enlargements, a small tumour will soon cause pressure effects, and moreover an affection of the specialized tissues supplied by these regions, as of the muscles of the hand, will be noticed early. In other regions, and especially in the region of the conus and cauda equina, where the vertebral canal is spacious, a tumour may attain large size, yet cause few symptoms.

In most parts of the cord the effects of a tumour are for a long time limited to one or two segments. In the lumbar, sacral, and coccygeal regions, however, where the segments are crowded together, the effects are more widespread.

In the upper cervical region a tumour may affect the lower cranial nerves, and cause difficulty in swallowing or in articulation, or it may compress the origin of the phrenic nerve and embarrass respiration. In the cervical and upper thoracic region a tumour may interrupt fibres going to the cervical sympathetic chain and lead to dilatation of the corresponding pupil and enophthalmos.

**Effects of Obstruction of the Spinal Canal.** A spinal tumour or any other lesion (tuberculous, inflammatory, etc.) that obstructs the free flow of fluid down the spinal canal produces characteristic effects. These effects, which may be recognized by hydrostatic, chemical, and radiological observations, are often in settling the nature and the site of obstruction.

(1) *Hydrostatic Tests.* If the tumour is situated at the usual level for lumbar puncture, attempts at aspiration at this site will fail to obtain fluid. Usually the tumour is situated above the level of lumbar puncture, and then the pressure of fluid is usually low, though occasionally (perhaps from some valvular action) it is raised. Alterations of pressure may be demonstrated most clearly by the so-called Queckenstedt test, which depends upon the fact that temporary compression of the jugular veins, by increasing the intracranial tension normally causes an immediate spurt of fluid from the lumbar puncture needle; any obstructive lesion in the spinal canal tends to prevent this and if the obstruction is sufficiently complete the rise of pressure is diminished or absent. A modification of the same test is that of Ayer, which consists in performing simultaneous lumbar and cisternal punc-

ture When the jugular veins are compressed the pressure at the two needles may be compared, and any delay in transmission of the wave of pressure may be recorded

(2) *Chemical Tests* Chemical examination of the fluid obtained by lumbar puncture is often of value Stagnation of fluid below the tumour combined with transudation from dilated meningeal veins causes an increase in the protein content and a yellow discoloration The protein of cerebrospinal fluid normally amounts to less than 40 mgm. % and any increase above 50 mgm. % without corresponding increase in cells may be regarded as abnormal The combination of massive coagulation of the fluid, and a yellow discoloration (xanthochromia) constitutes From's syndrome When fully developed it is strong evidence of obstruction within the spinal canal though not necessarily by a tumour

(3) *Radiological Tests* Radiological examination is sometimes necessary for the exact localization of the tumour though often this can be made from simple neurological examination The examination is assisted by the intrathecal injection of lipiodol, which is opaque to X rays Lipiodol of light specific gravity may be introduced through a lumbar puncture needle, or heavy lipiodol may be injected into the cistern As the oil ascends or descends the canal part or all of it may be arrested at the site of obstruction

### ANTERIOR POLIOMYELITIS (Infantile Paralysis)

In virtue of its paralytic sequelæ poliomyelitis is the commonest of all causes of crippling in childhood and constitutes a problem of vast importance, both surgically and epidemiologically

At its inception it has the characters of a general infection The main incidence falls upon the central nervous system but changes occur also in other parts of the body, particularly in lymphoid tissues and parenchymatous organs which show various degrees of cloudy swelling and degeneration

There is ample evidence that the disease is infective and the causal agent a filter passing virus, which probably gains access to the body through the mucous membrane of the upper air passages It is inferred that the virus reaches the central nervous system directly along the fibres of the olfactory nerve, but a blood borne infection is more likely Flexner and Noguchi have shown that such a virus can be isolated from the spinal cord of patients and that when injected into monkeys reproduces the characteristic lesions Most cases of poliomyelitis occur sporadically, but not infrequently there are minor epidemics which are especially apt to occur during the summer and autumn Children may be affected at any age but the disease is rare in infancy and the great majority of cases occur between the third and fifth years There is a well marked natural immunity to the disease and it has been estimated that only about 2% of the population are susceptible A single attack gives lasting immunity, and for many years afterwards the serum contains anti bodies The serum of a convalescent patient may be used in the treatment of the acute phase

The pathological changes in the central nervous system are most obvious in the anterior horns of the spinal cord at the level of the

lumbar enlargement, and consequently the most drastic and most lasting effect is motor paralysis of the lower extremities. In the acute phase of the disease, however, the posterior columns are also affected, and this may give rise to pain and tenderness in muscles and joints which may obscure its recognition. At first the affection is often widespread throughout the cord and even the brain, and may lead to a fatal result from implication of vital centres.

At an early stage the signs of inflammation appear both in the meninges and in the substance of the cord itself. Microscopically, the striking feature is the presence of lymphocyte collections, especially in the perivascular spaces in the anterior horns of grey matter, and along with this there is extensive oedema as well as congestion and petechial hæmorrhages. These changes are not uniformly distributed but are patchy, and consequently some nerve cells are affected, whilst adjoining ones escape. The nerve cells may be affected directly by the toxins of the virus, but more probably they succumb to the mere mechanical effects of oedema and ischæmia. After the acute phase a focal sclerosis of the neuroglia may damage the nerve cells still further.

The cerebrospinal fluid becomes altered early in the disease, and its examination has a certain diagnostic value. In the first week the characteristic feature is an excess of lymphocytes, and later there is an increased globulin content. Fehling's solution is usually reduced. As a rule the fluid is clear and colourless and does not show any great increase of pressure.

The paralytic lesions are almost invariably of lower motor neuron type, the muscles are therefore flaccid and tend to waste, and their reflexes diminish. At first the paralysis may be widespread, but since the nerve cells are not destroyed, merely compressed, a remarkable amount of restitution of function usually occurs. Almost always, however, some residual lesion remains, and subsequently leads to deformity. Generally this residual paralysis is restricted to one lower extremity, and very often merely to one group of muscles, such as the peroneal or anterior tibial or quadriceps group. The usual deformity is therefore some form of talipes with drop-foot and instability of the ankle. Sometimes the quadriceps femoris group of muscles is affected, and the knee thus rendered unstable. Paralysis of the abductors at the hip is not uncommon, it is very disabling as it prejudices the maintenance of the erect posture. In addition to the muscle atrophy there are trophic disturbances, and the growth of the limb is impaired. Less often an upper extremity is involved, and then the muscles around the shoulder are especially liable to atrophy. In other cases both legs or three or four limbs and the trunk are affected, but even then the paralysis in any one limb is rarely complete, and some few fibres in certain muscle groups remain active. This capricious distribution has important practical results, for the healthy muscles, being unopposed, contract, and often draw the limb into positions of disabling deformity.

#### TUMOURS OF THE NOTOCHORD: CHORDOMA

The notochord, the primitive entodermal axis around which develops the mesoderm of the vertebral column, normally disappears almost

completely in early foetal life. Occasionally a portion of its cephalad extremity persists at the base of the skull, and in infancy traces may be found as the nucleus pulposus in any intervertebral disc and in the region of the coccyx. The persistent rudiment at the base of the skull is said to be present in about 1% of all autopsies; it forms a small gelatinous button-like protrusion adherent to the cerebral aspect of the base of the skull, usually in the mesial plane of the clivus, 1 or 2 cm. behind the posterior margin of the pituitary fossa; it is without clinical significance except as a possible starting point for tumours.

Chordoma is a rare tumour of low malignancy derived from notochordal remnants. It usually occurs at one or other end of the body, in the spheno occipital or sacro-coccygeal regions. It tends to grow slowly, infiltrating and destroying surrounding tissues and even bone. It attains large size and eventually causes death. Exceptionally it grows rapidly, but it rarely gives rise to metastases.

The spheno occipital chordoma generally arises in adults of thirty to forty years. Springing from the cerebral aspect of the clivus, it projects upwards into the cranial cavity and, eroding the bone, expands into the nasopharynx, the orbit, or the air sinuses. The sacrococcygeal chordoma may arise either in front of or behind the bones. It forms a slowly growing tumour which eventually may attain large size. When situated in front of the sacrum it tends to obstruct the gut and leads to interference with micturition.

Typically, the tumour is encapsuled and broken up into lobules by very dense fibrous trabeculae. The parenchyma is composed of bluish-white gelatinous tissue, often haemorrhagic, and there are usually cysts containing mucoid fluid.

Microscopically, there are alveolar masses of cells of epithelial type, sometimes lacking clear definition and resembling a syncytium. The most characteristic feature is the presence of large vacuoles, both in the cytoplasm and



FIG 137 Chordoma. The tumour is composed of alveoli of vacuolated epithelial cells containing globules of mucin.

(By courtesy of Dr W A Alexander and Mr J W Struthers.)

in the nuclei, so that the cells become swollen or bladder like (physaliphonic). The vacuoles result from intracellular mucin-formation, and as the cells increase in size they discharge the mucin into the

intercellular substance In some tumours, especially those of slow growth, the greater part of the tissue may be replaced by masses of gelatinous material Some parts of the tumour may assume sarcomatous characters

Clinically, it is important to recognize the tumour, for though complete extirpation is not to be expected, local removal of the tumour or aspiration of mucoid contents has been followed by remarkable remission of the pressure effects

### SACRO-COCYGEAL TUMOURS, CYSTS AND FISTULÆ

The complex nature of its development and the rudimentary structures which abound in its neighbourhood render the sacro-coccygeal region very subject to the growth of tumours and cystic swellings These are almost always congenital and are usually found in female infants, they are often incompatible with life, and when large may even cause impediment to parturition

Classification is difficult, for the histological picture is remarkably varied The simplest grouping recognizes two principal types, those due to anomalous development of the early embryo, and those arising from the persistence and growth of structures which under normal circumstances atrophy and disappear In addition, inclusion dermoid cysts may occur in this region

(1) *Anomalous Development in the Early Embryo* This gives rise to various forms of parasitic inclusions, ranging from a solid teratoma up to a completely formed limb—an incomplete parasitic twin It is believed that two embryonic areas form in the single blastomere, the one developing completely as the autosite, the other remaining ill formed as the parasite Two principal varieties of parasitic inclusions may be recognized —

(a) *Parasites* composed of definite organs or their rudiments, portions of viscera, bones, or well formed extremities These are rare in man and apart from the deformity give rise to no complications

(b) *Sacro-coccygeal teratomata*, solid or cystic tumours arising either in front of or behind the sacrum and coccyx. These tumours are at first encapsuled and they may grow slowly or remain unchanged, but sometimes they assume sarcomatous characters Microscopically, they have the features of a teratoma and include areolar and fibrous tissues, areas of cartilage, and mucoid, nervous and osseous tissues

(2) *Persistence of Rudimentary Structures* In the complex development of the hind part of the body there are several structures which may later give rise to tumours, cysts or fistulæ Ventrally, there are the neurenteric canal, the post anal gut, and the proctodæal membrane The neurenteric canal is a tiny channel which in the early weeks of intra uterine life connects the lower end of the spinal canal with the posterior termination of the gut The portion of gut with which it communicates lies posterior to the point of communication between the gut and the invaginating proctodæum—post anal gut Tumours developing from these tissues are situated ventral to the sacrum and coccyx, though they may later be displaced downwards or dorsally



They are composed of closed vesicles lined by columnar cell glandular epithelium and they contain ropy mucus

*Congenital post anal cysts and sinuses* (pilonidal sinus) arise in the median plane in relation to the skin dimple at the tip of the coccyx and are due to a defect in embryonic development. They are believed to arise from either a remnant of the spinal canal known as the coccygeal vestige, or (and more likely) from excessive traction on the skin caused by the retrogression of the tail bud (traction dermoid). The sinus is lined by skin, and hair may project at its orifice, and as a result of exudation into its lumen one or more small nodular cysts may develop subcutaneously. From the proximity of the sinus to the anus infection and suppuration are apt to occur and fresh sinuses may be established at a higher level or laterally. The condition is chiefly of importance because it is often confused with fistula in ano. As the sinus is lined with skin healing cannot be secured unless the entire epithelial wall is excised.

It is worth noting that a similar condition may occur in a barber's hand from accidental puncture.

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## CHAPTER XV

### DISEASES OF THE PERIPHERAL NERVES

#### NEURITIS DUE TO PRESSURE

APART from solution of continuity, the most important surgical lesions of the peripheral nerves are those due to pressure—*pressure neuritis* or *neuralgia*. There are several well known examples of such neuritis which deserve individual consideration (1) brachial neuritis due to pressure of developmental structural abnormalities at the root of the neck (2) median nerve compression at the wrist, (3) traumatic ulnar neuritis and (4) sciatica.

#### NEURITIS CAUSED BY STRUCTURAL ABNORMALITIES AT THE ROOT OF THE NECK

##### (Thoracic Outlet Syndrome Costo-clavicular Syndrome)

The main nerve trunks and the subclavian artery may be compressed as they leave the thorax and traverse the root of the neck. Apart from central causes such as spondylitis scoliosis, and herniation of an intervertebral disc the usual causes of nerve compression are developmental derangements of the ribs and the scalene muscles.

In the past, undue emphasis has been placed upon osseous abnormalities and too little account taken of the part played by the related muscles and not least the aggravating influence of abnormal posture.

The underlying structural abnormalities responsible for pressure on the brachial plexus and subclavian artery are many and varied and their mode of action is not interpreted alike by all observers. In most instances nerve pressure is most conspicuous, though sometimes effects referable to compression of the subclavian artery predominate, or there may be combined features.

Broadly the structural abnormalities responsible for neurovascular compression are of two kinds—(1) rib abnormalities, and/or (2) abnormalities of muscles and ligaments.

(1) **Rib Abnormalities** The two chief rib abnormalities are (a) supernumerary (or cervical) ribs and (b) an abnormal or rudimentary first rib.

A cervical rib is present on one or both sides in about 8% of subjects. In only about 5% of instances is it responsible for symptoms and then most often in women (8/1) and especially on the right side. The rib arises in connection with seventh cervical vertebra and transverse process (rarely the sixth). Its formation and mode of articulation and relationship to nearby structures show great variation. In the type which commonly produces symptoms, the rudimentary rib is used with the vertebral body or transverse process and projects only slightly into

the neck, but is prolonged as a tight, fibrous cord which gains attachment to the periosteum at some part of the first rib. Sometimes it is more completely developed with a definite bead, neck, and tubercle, and then may articulate with the vertebra and laterally with the first rib or cartilage or occasionally the sternum. It is frequently welded to the first rib by an irregular synostosis.

The shape of a cervical rib varies. In some it is long, thin and pointed, in others it is broad and flat and resembles the first rib and may be grooved by the subclavian artery and the lower part of the brachial plexus. The direction of the rib is important, because if it merely projects horizontally in a lateral direction it is unlikely to come in contact with the brachial plexus or the subclavian artery, whereas if it curves forward and is lacking in mobility these structures acquire a more intimate relationship with it. If the rib extends towards the first costal cartilage the scalenus anterior muscle in whole or part may be attached to it.

*Abnormal or rudimentary First Rib.* The first rib may be of slender structure, and its axis, normally flat on all aspects, may be deviated inwards so that its medial border is unduly sharp and may predispose to undue pressure on the first thoracic nerve root. Wood Jones attributed this

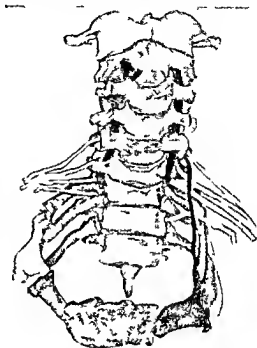


FIG 138 Dissected specimen of bilateral cervical ribs. The right cervical rib articulates anteriorly with a protuberance from the first thoracic. On the left side the scalenus anterior muscle is seen inserted into the tip of the cervical rib which is prolonged forwards to the sternum by cartilage. The relation of the brachial plexus to the cervical ribs is clearly shown.

(Museum of Royal College of Surgeons of Edinburgh)

type of rib development to the suppressive effect of post fixation of the brachial plexus, i.e., an unusually large contribution to the brachial plexus from the first or even second thoracic nerve root.

(2) *Abnormalities of Muscles and Ligaments.* It was noted above that a tendinous band may extend forwards from the lateral extremity of a cervical rib and that the brachial plexus may impinge upon it.

The scalenus anterior muscle is in intimate relation to the second part of the subclavian artery and the cords of the brachial plexus. Slight variations in the muscle especially in association with rib and postural defects may be responsible for constrictive effects. The scalenus anterior is most often at fault, although when the insertion

of the scalenus medius is carried unusually far forward it may involve the plexus. The V shaped cleft between the scalenus anterior and the first rib where the subclavian artery and the brachial plexus converge is relatively narrow—especially in certain postures—particularly hyperextension of the neck.

In rare instances vestigial structures may persist and be responsible for nerve compression—thus an independent muscle strip—the scalenus pleuralis—may arise from the tubercle of the seventh transverse process to gain insertion into the inner border of the first rib and pleura. In some instances the muscle is replaced by a ligament (lig. costo pleuro vertebrale).

The lowest trunk of the brachial plexus where it impinges on a rib or muscle is often notched. Sometimes it is the seat of thickening and in others it is oedematous and congested. There is no evidence that the *grev. ram. communicantes* are unduly affected. The subclavian artery, although often unduly high in the neck, may be normal but in a number of instances it is the seat of localized atheroma or even calcification. Intramural thrombosis is likely to occur and may extend peripherally or emboli may be detached and reach the smaller branches in the limb. Sometimes the artery is the seat of fusiform dilatation immediately distal to the site of constriction. It has been ascribed to weakening of the vessel wall from interruption of *vasa vasorum* though such evidence is lacking.

**Predisposing Factors** The predisposing factors in compression include any cause which tends to stretch the lower trunk of the brachial plexus over either a rib band or muscle border—as in certain occupations. In some instances there is an obvious loss of muscle tone which exerts a dragging effect and in this connexion it is of interest to note that symptoms have sometimes appeared after the accessory nerve has been divided. It has been suggested that the dropping of the shoulder and elongation of the neck that occur in adolescence especially in women may predispose to stretching of or pressure on the plexus and possibly this is a reason for women suffering from pressure neuralgia more often than men. It is exceptional for symptoms to appear before the age of fifteen most frequently they appear about the age of twenty.

**Effects** Pressure effects are the result of involvement of the sensory and motor fibres in the lowest trunk of the brachial plexus.

Sensory disturbance is manifested by pain along the ulnar border of the forearm, and by paresthesia and later small areas of anaesthesia in this region and sometimes the finger tips. Occasionally it occurs on the radial side of the forearm and is then probably of other origin (*v. infra*).

Motor disturbance is evidenced by difficulty in executing delicate movements and by clumsiness in lifting small objects. Paresis of the intrinsic muscles of the hand may occur and it may affect the muscles supplied either by the median or the ulnar nerve. The paresis does not follow the nerve distribution strictly—for example the adductor pollicis brevis and opponens pollicis may be affected yet the flexor pollicis also probably supplied by the median nerve may escape. At a late stage a typical *main-en-griffe* may develop.

Vasomotor phenomena are common, so that the hand and fingers

may be cold and of a livid blue colour. When gangrene of the fingers has occurred it is probably the result of emboli detached from the subclavian artery. The vasomotor and trophic changes were at one time attributed to pressure irritation of the grey rami incorporated in the lowest trunk of the brachial plexus. It is much more likely that constriction of the subclavian artery and local changes in its wall and lumen are responsible, and certainly in these cases in which vascular phenomena predominate, changes can be demonstrated. There is evidence that detachment of small thrombi from the subclavian artery and progressive intra arterial clotting are responsible for the ischaemia in the hand and forearm. In some instances the whole of the main vessel—subclavian and brachial—may be obliterated.

**Costo-Clavicular Compression** It is well known that in certain positions of the shoulder the radial pulse is diminished or completely obliterated. It occurs particularly when the arm is held firmly to the side with the shoulder depressed, and with even greater frequency when the shoulder is braced squarely back. It has been observed that in certain occupations or pursuits there is evidence of compression of both the subclavian artery and vein and of the brachial plexus as well. The resulting paræsthesia numbness of the hand has been attributed to compression between the clavicle and first rib—the so called Costo clavicular syndrome. It is open to doubt whether the clavicle can be approximated close enough to the first rib to exert pressure. It is more likely the drag on the nerve cords and vessels is caused by the tendinous border of either the scalenus anterior or medius, against which they may be pressed when the shoulder is braced back.

In rare instances the axillary artery is compressed by the grip of the two heads of the median nerve especially in downward traction of the arm. The constriction may be sufficient to obliterate pulsation distally, and to produce ischaemic manifestations in the hand.

**Median Nerve Compression at the Wrist** Compression neuritis of the median nerve may result from some obvious cause such as fractures at the lower end of the radius or of the carpal bones which narrows the carpal tunnel. It may, however, occur in the absence of any obvious structural abnormality.

The condition has been observed most often in middle aged women compelled to do heavy manual work. One hand is usually affected, but the other may suffer later. Compression is evidenced by burning and tingling sensation in the cutaneous distribution of the nerve, with impaired sensitivity to touch and pain. The small abductor, and the opponens pollicis muscles are weak and wasted.

It is believed that the action of repeated extension entailed in certain occupations abrades the nerve in the carpal tunnel, or raised the tension within, is sufficient to cause compression. Relief is secured by division of the transverse carpal ligament. The median nerve is the seat of oedema over a distance of about one inch proximal to the ligament.

#### Traumatic Ulnar Neuritis

Apart from pressure of a cervical rib, the commonest cause of neuritis of the fibres of the ulnar nerve is injury to, or pressure upon

the nerve at the elbow joint. In most cases the condition follows a fracture in the region of the medial epicondyle, or it may follow arthritis, dislocation, exostosis of the ulna, contusion, and abnormal mobility of the nerve associated with recurrent displacement.

Platt, in an analysis of 252 cases of injury in the region of the elbow joint, found that neuritis developed in 9 instances, which indicates that the complication is relatively rare.

Ulnar neuritis sometimes develops soon after receipt of a fracture or other injury (recent neuritis), but more often there is a very long interval, even decades (delayed neuritis).

Recent neuritis is usually associated with a fracture of the medial epicondyle of the humerus or, in young subjects, with separation of its epiphysis. The neuritis may be due to contusion of the nerve as it lies posterior to the epicondyle, or to pressure by callus. In cases associated with separation of the medial epicondyle the signs and symptoms are often characteristic. There are swelling, and bruising, and tenderness over the medial side of the elbow, and a variable amount of numbness and anesthesia in the skin of the ring and little fingers, whilst movement of the interossei muscles may be impaired.

Delayed neuritis usually develops in adult life. Fracture at the elbow joint is the most common predisposing cause, and it is characteristic of this form that many years elapse (it may be as many as thirty) before signs or symptoms appear. In some cases there is evidence of an old fracture which had occurred so early in childhood and was so little disabling, as to leave no recollection of the accident.

In most cases the neuritis has been associated with a fracture of the lateral epicondyle of the humerus, in which there have been upward displacement of the separated fragment and faulty union in the position of cubitus valgus, in consequence of which the ulnar nerve is stretched or chafed. Probably changes in the elbow joint affecting the shape of the medial epicondyle determine the onset of neuritis.

When seen at operation the nerve is usually red and shows a spindle shaped swelling composed mostly of fibrous tissue.

In this type of neuritis the motor fibres appear to be more vulnerable than the sensory, for there may be atrophy of the interossei and the hypothenar muscles with only slight disturbances of sensation.

#### Sciatica

Pain referred to the distribution of the sciatic nerve may result from lesions of the nerve itself or its roots—for example the pressure of a tumour or a prolapsed intervertebral disc—or it may occur as a reflex manifestation secondary to such sources of irritation as lumbar fibrositis, affections of the lumbo sacral spine and articulations and diseases of the pelvic viscera.

In recent years opinion has changed completely as to the relative frequency of the different causes of sciatica. Formerly much importance was attached to a true neuritis of the sciatic nerve, which was attributed to various types of toxæmia or occasionally to diabetes while among local causes particular attention was directed to such affections as sacralization of the fifth lumbar vertebra and arthritis of the lumbar,

lumbo sacral and sacro iliac joints. Now, on the other hand, there is general agreement that such lesions are unimportant and it is thought that, if gross organic disease such as spinal tuberculosis and malignant disease be excluded, sciatica is usually due either to fibrositis or to the pressure of an intervertebral disc. Some authorities would even go further and assert that the last mentioned lesion is the one responsible in a large majority of cases.

**Reflex Sciatic Pain.** It has been established beyond all doubt that pain in the sciatic distribution may be caused reflexly by painful lesions within the territory supplied by the posterior primary divisions of those roots whose anterior divisions constitute the sciatic nerve. This territory includes the lumbar muscles and fasciae, the intervertebral joints and the interspinous and supraspinous ligaments. Proof of this thesis was given by Kellgren, who observed that pain referred to the sciatic distribution can be evoked by injection of hypertonic (6%) sodium chloride solution into the supraspinous ligaments.

According to some workers, fibrositis of the lumbar muscles and fasciae is a common cause of sciatica while spinal arthritis and postural strains in the lumbo sacral region are regarded as less common causes. In support of the importance of fibrositis it is claimed that often there is a history of 'rheumatic' affections, that the pain often develops after a chill or exposure to cold or damp, that tender nodules can often be demonstrated, and that the injection of local anæsthetic into such nodules gives prompt relief.

**Sciatic Pain and Prolapsed Disc.** Prolapse of an intervertebral disc (see p. 298) is now regarded as one of the commonest causes of sciatic pain. The fifth lumbar root is the one affected most commonly. It may be stretched as it passes over the protrusion or compressed as it emerges from the intervertebral canal. Rarely the same effect is produced by hypertrophy of the antero lateral margin of the ligamentum flavum.

The root pressure may lead to motor and sensory changes and to disturbance of the tendon reflexes. The muscles of the thigh and leg commonly are wasted, but there is little loss of power apart from voluntary limitation of movement due to pain. Sensory disturbances are slight and usually are limited to numbness and paresthesia over the dorsum and lateral margin of the foot. The ankle jerk is diminished in a considerable proportion of cases.

The pain of sciatica appears to be due partly to root irritation and partly to muscle spasm, as has been shown by Elliott by studies with the electromyograph. Accentuation of the pain by the straight leg raising test is due partly to traction upon the nerve root and partly to stretching the spastic hamstring muscles.

### Causalgia

This term was introduced by Weir Mitchell to describe a severe intractable burning pain occurring after injury to a nerve trunk. It is sometimes applied more widely to painful amputation stumps, tender scars, etc.

True causalgia follows a partial injury to a nerve and is rare except in the median and posterior tibial nerves. The pain is felt diffusely in

the area of distribution of the nerve. It may occur spontaneously or be precipitated by touch, by extremes of heat or cold, or by emotional stimuli. It starts a few hours after the injury and may persist, in varying degree, for years. In severe cases secondary neurotic manifestations are common.

On examination there is acute hyperæsthesia in the affected area which is atrophic, with shiny red warm skin, ridged nails and other "trophic" changes. The bones may show osteoporosis similar to Sudek's atrophy.

In seeking the explanation of causalgia it must be remembered that the nerve injury is always incomplete, that the pain is aggravated by sympathetic stimuli and relieved by sympathectomy, and (most remarkably) that in some cases relief can be obtained by procaine block of the nerve distal to the point of injury. According to Lewis, impulses originating at the injury are conducted in sensory fibres distally (anti-dromic) and there set up a hyperalgesic state, perhaps by liberating a histamine like substance, pain originating in this hyperalgesic area is then conveyed to the sensorium through intact fibres in the normal way. Recently Doupe and his colleagues have suggested that a breakdown of insulation at the site of injury leads to a short circuit or 'artificial synapse' whereby action currents travelling distally along sympathetic nerves overflow to adjacent sensory fibres and thus back to the sensorium where they are interpreted as pain.

## TUMOURS OF PERIPHERAL NERVES

### Structure and Development of Peripheral Nerves

The individual fibre of a nerve consists of an *axis-cylinder* (or *axon*) which is usually encased in a myelin sheath outside which is a continuous

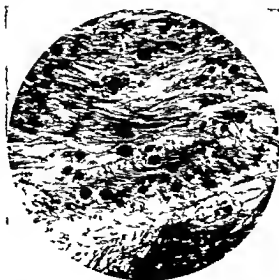


FIG. 179. Section of ganglioneuroma stained by Bielchowski method. Note ganglion cells and non-medullated nerve fibres.



syncytium of cells, the *neurilemma sheath* (of Schwann) Nerve fibres are embedded in a fine reticulum—the *endoneurium*—are grouped cable like by the *perineurium*, and maintained as a trunk by the *epineurium*

The axon is a prolongation of a nerve cell, myelin (if present) is a product of the cell, and the neurilemma a derivative of the neuroectoderm emerging from the neural crest, as also, probably, are the supporting tissues endoneurium and perineurium

Embryological and cytological researches, and Harrison's well-known experiments on frogs, make it certain that the epithelium of the neural crest is the progenitor, *inter alia*, of the posterior root ganglia, the sympathetic nervous system (including the suprarenal medulla), the investments of nerves and the leptomeninx and choroid plexus

There is accumulated evidence that many tumours classed formerly as false neuromata are composed of undifferentiated nerve elements, and that the division of tumours into true and false neuroma may be discarded in favour of separate consideration of each well-defined type There are well differentiated tumours in which the neural character is obvious, some in which it is supportable, many in which it is debatable. The following types will be considered :—

### (1) Neurinoma (False Neuroma)

Thus tumour was formerly regarded as a pure fibroma arising from the nerve coats, but its origin from the neurilemma sheath is now conceded except by a few It is usually single, small, lightly encapsuled by the perineurium, and easily separated from the affected nerve trunk, it is, unlike a pure fibroma, prone to cystic degeneration It usually affects nerves of the upper extremity and those in the subcutaneous tissues It may occur intraspinally or intracranially

Histologically, the major part of the tumour is composed of wavy bands of collagen, interspersed with elongated nerve fibrils Whorls of fibres may be present, and in these zones clumping of the nuclei may occur to produce a familiar "palisade" effect A reticulum stain displays crowds of fine fibrils which, it has been concluded, arise from the neurilemma sheath rather than from the endoneurium

### (2) Neurofibromatosis, (von Recklinghausen's Disease)

This condition is regarded as a developmental disorder of the supporting tissues of nerves rather than an example of new growth, although tumours (in the anatomical sense) may be one of its more obvious features

Histologically, the characteristic feature of the disorder is proliferation of tissues, especially those of the nerve sheaths, in which both the fibrous and the neurilemmal elements participate in different degree and with remarkable irregularity In the tumour formations myxomatous changes are of common occurrence

The disease, which is often familial, usually begins in adolescence, and frequently the first evidence is localized areas of pigmentation in

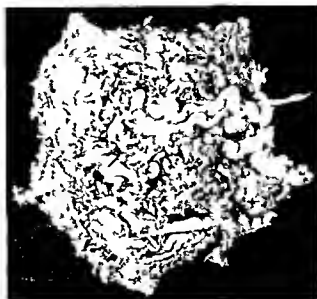


FIG. 140 Plexiform neuroma removed from the subcutaneous tissues of the lateral thoracic wall of a male child aged ten years. The tumour had gradually increased in size during five years. Diffuse neurofibromatosis and scoliosis were also present.

(Museum of Royal College of Surgeons of Edinburgh.)

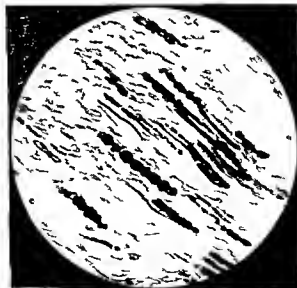


FIG. 141 Plexiform neuroma. Microscopic section stained by the Weigert-Pal method (High power). The tissue surrounding the nerve fibres is partly fibrous and partly of neurilemma or gria.

(Museum of Royal College of Surgeons of Edinburgh.)

the skin followed later by overgrowth of nerve trunks or tumour formations large or small localized or widespread. Any of the nerves in the body, peripheral cutaneous sympathetic and cranial may be

affected In some examples of the disease there are glomata in the brain in others multiple intrathecal tumours In rare cases bilateral acoustic neuroma occurs, sometimes with tumours of the meninges and choroid plexus The final outcome of the disease depends on the size and site of the tumours and upon the proclivity to malignant change

The common ancestry of the different lesions is suggested by their complexity and remarkable blending in individual cases and the striking variations in groups of cases The various lesions, will be discussed under the following headings —

- (a) Generalized neurofibromatosis
- (b) Plexiform neuroma
- (c) Cutaneous neurofibromatosis  
(multiple soft fibromas of skin  
molluscum fibrosum)
- (d) Elephantiasis neuromatosa
- (e) Bilateral acoustic neuroma
- (f) Primary sarcoma of nerves

(a) Generalized neurofibromatosis varies greatly in its distribution Any of the cerebrospinal nerves may be affected, as well as the ganglia on the posterior nerve roots, and the nerve fibres within the muscles and bones The nerve roots within the spinal canal may also be affected and this most often occurs in the cervical region and in the cauda equina The affected nerves are diffusely and irregularly thickened so that small twigs may assume giant proportions, and, at intervals in the course of the nerves, growth may be exaggerated so as to form tumour like swellings

If one of the affected nerves is examined in transverse section the most notable change is the overgrowth of connective tissue within the primary bundles of the nerve Certain bundles may be affected at one point and may be exempt at another Some bundles may escape completely while others are markedly affected The nerve fibres appear to traverse the substance of the swelling The fibromatosis affects the endoneurium (the delicate connective tissue between the individual fibres of a nerve bundle) whereas the perineurium and the epineurium (outer sheath) are unaffected There is no proliferation



FIG 149 Sarcoma of the posterior tibial nerve arising on a basis of neurofibromatosis Note the greatly thickened nerve which emerges near the lower extremity of the tumour The other nerves of the limb showed the features characteristic of neurofibromatosis

(Department of Surgery, University of Edinburgh)

of the nerve fibres, and the only change which they undergo is compression and elongation. There is no degeneration and, therefore, no sensory or motor changes are observed.

In a considerable proportion of cases one of the tumours assumes malignant characters (so called secondary malignant neuroma). Such transformation, by which the tumour assumes the features of a rapidly growing sarcoma, often follows injury or an attempt at removal.

(b) A plexiform neuroma is the result of diffuse fibromatous thicken-



FIG 143 Cutaneous neurofibromatosis. Note the large tumour of the right buttock and the patches of pigmentation. The woman's father suffered from neurofibromatosis.

(Museum of Royal College of Surgeons of Edinburgh.)

ing of the branches of a nerve, the resulting swelling is palpable beneath the skin and may resemble thrombosed tortuous vessels. In more than half the cases there are manifestations elsewhere of generalized neurofibromatosis.

The commonest situations for a plexiform neuroma are the subcutaneous tissues of the head and neck, the large nerves of the extremities, and the autonomic plexus of the abdomen. The skin over the tumours may show localized overgrowth and pigmentation, and the masses of thickened skin may become pendulous.

(c) Cutaneous neurofibromatosis (*molluscum fibrosum*) gives rise to multiple, soft, fibrous swellings of the skin, which vary in size from a

to a plum or larger. They arise in connexion with the elements of cutaneous nerves. They may be sessile or peduncled and are most numerous over the breast, back and abdomen. They are very abundant on the scalp and the extremities, but the face of the hand and the sole of the foot escape.

A majority of cases of cutaneous neurofibromatosis there is thickening of the skin, either in spots or diffusely disposed, and café au lait spots may be present. In addition, neurofibromatosis of peripheral nerves is present in a large proportion of cases.

**Elephantiasis Neuromatosa.** All intermediate grades may be found between molluscum fibrosum and elephantiasis neurofibromatosa. The two may coexist, and may be associated with generalized thickening of the nerves, and with plexiform neuroma.

The disease generally affects one of the extremities, especially the lower. It is of congenital origin and begins in a brown spot or mole, or in an area of neurofibromatosis, which may or may not be pigmented or hairy. The increase in size of the affected part is gradual, but may occur abruptly at puberty.

The skin and cellular tissues are enormously thickened and the subcutaneous fat is replaced by fibrous tissue. The subcutaneous tissues present an oedematous, glistening, greyish white appearance, in places they are soft and gelatinous, in others they are white, dry and fibrous. A variable number of tumours, isolated or in strings, may be present.

#### (e) Bilateral Acoustic Neuroma

In rare instances neurofibromatosis may be associated with bilateral acoustic nerve tumours. The disease has a striking familial incidence showing itself as a Mendelian dominant. Tumours of the dura and the choroid plexus may sometimes coexist.

**(f) Primary Sarcoma of Nerves.** A sarcoma usually originates in a nerve already the seat of fibromatosis, and the resulting tumour is usually of a spindle-cell or myxosarcomatous character. It possesses no appearances suggesting its neural origin. The tumour grows rapidly, is markedly radio resistant and recurs promptly after local removal. Metastasis is to be expected in at least 20% of cases.



FIG 144 Elephantiasis neuromatosa  
(Museum of Royal College of Surgeons of Edinburgh)

### (3) Ganglioneuroma

This is the most highly differentiated type of nerve tumour and arises in connexion with the sympathetic trunks in the abdomen, neck and the mediastinum. It commonly occurs in relation to the suprarenal gland. Histologically it is composed of uni or multi polar giant cells in varying numbers scattered amongst nerve fibrils which may or may not be myelinated (Fig. 139). In rare instances ganglion cells are absent and the tumour consists of masses of amyelinated nerve fibres a feature which suggests that nerve fibres may proliferate without the trophic influence of ganglion cells. Such tumours have been found in multiple form in the medulla cord and pia mater and in the mediastinum.

A ganglioneuroma usually occurs in childhood. It varies in size from a pea to larger than a melon. Some specimens are lobulated others smooth and rounded. In appearance it resembles a fibroma or a lipoma. It is unattended by signs suggestive of a nervous origin or structure and such pathological effect as it produces is due to pressure. Pressure effects may be referred to the opposite side.

### (4) Sympathicoblastoma (Neuroblastoma)

This tumour develops from immature cells of the sympathetic nervous system and is therefore common in the first years of life. There is great variation in the structure of the tumour. The most undifferentiated (which nearly always occurs in the region of the kidney) is composed of lymphocyte like cells often arranged like staphylococci and intensely argenteophilic. Rosette formations may be present at the periphery of the tumour but there are no fibrils. Such tumours are rapid growing, reach a large size and metastasize widely. The more differentiated types (which also are commonest in relationship to the suprarenal gland but may occur in the neck, the coeliac ganglion and other sites) are usually smaller and are composed of more differentiated cells often of larger size than in the undifferentiated with more numerous rosette formations, nerve fibrils, axis cylinders and ganglion cells. They may metastasize by the blood or lymph channels. It has been observed repeatedly that if ganglion cells are present in the parent tumour they are not found in metastases.

It has been observed that an undifferentiated tumour may during years gradually change its character and become differentiated i.e. the normal evolutions of the sympathetic nervous system are reproduced within the tumour.

### (5) Stump Neuroma

A traumatic or stump neuroma arises in the divided nerves after amputation. Occurrence of a small bulbous or fusiform swelling at this situation is normal but in some circumstances the neuroma assumes a large size especially if there has been infection.

The bulbous swelling consists of fibrous tissue newly formed unmyelinated nerve fibres in irregular formation and a syncytium of cells derived from the neurilemma sheath.

Bulbous enlargement of the nerve trunks may also follow repair of a nerve after division, and prolonged irritation, as in traumatic ulnar neuritis

#### (6) Glomal Tumour (Glomangioma)

This is a tumour of one of the cutaneous glomera, the specialized arterio venous anastomoses which are believed to have the effect of regulating the temperature and maintaining the circulation in peripheral parts exposed to cold

The normal glomus consists of a much convoluted, modified arteriole communicating directly with a vein. It has a rich perivascular nervous network and is believed to be capable of independent dilatation and contraction. It probably exercises its function by acting as a circulatory shunt, diverting blood into or away from the local capillary network.

The glomera are most numerous in the extremities, especially in the nail beds, and tumours of the glomera are also more common in these sites. The tumour is of slow growth and encapsuled. It may be symptomless or give rise to pain of a burning or bursting nature, originating in the tumour and sometimes radiating widely.

Pain is most common in subungual tumours, and may be brought on by pressure or light touch, or even by a change of temperature.

Microscopically the tumour is an angioneuromyoma. There are cavernous blood spaces containing red cells or thrombus, thick walled blood vessels showing proliferation of the muscle cells of the media, and numerous nerve twigs bearing hyperplastic perineurium. A characteristic feature is the presence of masses of *glomus cells*, cuboidal cells normally found beneath the endothelium of the vascular channel of the glomus. In the tumour these cells lie in coherent perivascular sheets. They are of uniform appearance, cuboidal in shape, with rounded hyperchromatic nuclei and distinct limiting membranes.

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# CHAPTER XVI

## DISEASES OF THE THORAX

### DISEASES OF THE PLEURA

#### PNEUMOTHORAX

KNOWLEDGE of the phenomena of pneumothorax in its various forms is essential for the proper appreciation of the effects of diseases of the lungs and pleura, and for the safe conduct of measures for their relief.

In health, the parietal and visceral layers of pleura are virtually in contact, for the pleural cavity is merely a capillary interval containing the film of lymph that moistens their surfaces. They are kept in contact by the distension of the lung under atmospheric pressure, and, owing to traction of the elastic tissue of the lung, the pressure of the potential pleural cavity is negative. During the inspiratory expansion of the chest the pressure diminishes till it is  $-7$  mm to  $-9$  mm of mercury at the end of inspiration, and air enters through the air passages and distends the lung still further to prevent a vacuum. In expiratory contraction of the chest, which is normally a passive movement, the lung shrinks by its inherent elasticity and partially evacuates its air, and the intrapleural pressure rises, but even at the end of expiration it does not equal the atmospheric pressure unless the glottis is closed. Deep inspiration may increase the negative intrapleural pressure to  $-30$  mm Hg and a forceful expiratory effort, such as coughing, produces positive readings as great as  $+50$  or  $+60$  mm Hg. The effects of alteration of the lung volume upon the intrapleural pressure will be considered more fully when the diseases that produce them are dealt with.

When air is present in the pleural cavity the condition is called pneumothorax. In open pneumothorax the air has free entrance and exit through a wound in the chest wall. In closed pneumothorax the air has neither entrance nor exit. In valvular or tension pneumothorax the air may enter but not escape from the pleural cavity. Each variety requires separate discussion.

#### Open Pneumothorax

Open pneumothorax may be the result of an injury to the thoracic wall or it may be produced deliberately in operations on the thoracic viscera. When an opening is made in the chest wall, air rushes into the pleural cavity, and the pressure within it rises. The lung—no longer responsible for the prevention of a vacuum—shrinks or collapses, owing to its elasticity, to the extent of the space occupied by the invading air. The only air effectual for oxygenating the blood is

that which enters by the air passages, and with ordinary respiration that would now be less than the normal requirement by the amount which enters through the opening in the chest wall, therefore, to maintain adequate oxygenation the patient must increase either the rate or the depth of respiration. In health a small opening is usually well tolerated, for only a little air enters, and a healthy system has strength to cope with the difficulty and can accommodate itself to the change. The normal requirement at each inspiration is approximately 500 c cm of air (the *tidal air*), whereas, the maximum amount a healthy adult can inhale is almost 4 000 c cm.

If the opening in the chest wall be large, the condition may be serious. The lung shrinks to one third or less of its original bulk, and the partial or complete collapse of the alveoli puts even more than two thirds of it out of effective action. Also, the other lung suffers reduction, for the mediastinal septum—in health (especially in young subjects) a soft and yielding partition made up chiefly of the heart and great vessels—is *pushed* by atmospheric pressure towards the sound side with each inspiration, to help to prevent the formation of a vacuum on that side. The septum moves back on expiration. This to and fro movement is accompanied by a mediastinal flutter, *i.e.*, a tremulous quivering of the structures in the septum, and since the heart is implicated in these movements they may be associated with a rapid pulse and shock. In addition, if a large open pneumothorax is long maintained the heat loss from the body is considerable, and as a result of the changed pressure relationship in the pleura, the return of venous blood to the heart may be impeded. In a large pneumothorax the air taken into the opposite lung is derived chiefly from the exterior, but also, to a small part, from the collapsed lung and during expiration the air is expelled through the trachea and partly into the collapsed lung, which becomes expanded to an extent proportionate to the expiratory effort. The movements of the lung on the side of the open pneumothorax are therefore reversed since the lung collapses during inspiration and expands during expiration (*paradoxical respiration*). The re-breathing of vitiated air which results from the paradoxical respiration leads to dyspnoea and demands violent respiratory movements to neutralize its ill effects.

These untoward effects of open pneumothorax are seldom witnessed except in severe injuries to the chest, especially if already there is a considerable degree of shock. They are not usually experienced in operations within the pleura provided the opposite lung is healthy and the patient's vital capacity<sup>1</sup> is fairly normal. A large opening into the pleura, in which the lung collapses, can be made with impunity. Even though the patient lies on the normal side respiration is undisturbed. A further safeguard against the possible ill effects of open pneumothorax is provided by the modern methods of anaesthesia which ensure delivery of so high a concentration of oxygen to the lungs that anoxæmia is not likely to occur if the airway is unobstructed.

<sup>1</sup> The *vital capacity* is a valuable indication of the respiratory reserve. It is defined as the maximum amount of air which can be exhaled after a maximum inhalation. On the average it is about 3,500 c cm.

### Valvular and Tension Pneumothorax

This form of pneumothorax may be urgent. It is usually attended by considerable shock and may lead to fatal asphyxia. The commonest cause is rupture of the wall of a superficial vomica in a tuberculous lung and the consequent establishment of a valvular communication between the air passages and the pleural cavity. The pleural cavity becomes greatly distended with air and sometimes purulent material. The wall of a tuberculous cavity may rupture during the treatment of pulmonary tuberculosis by artificial pneumothorax, especially if adhesions between the pulmonic and parietal pleura are situated over a cavity or an active focus of disease.

Other causes of tension pneumothorax are —

- (1) Rupture of an emphysematous bulla. This may take place in an apparently healthy person. Usually the air is rapidly absorbed, but recurrence, occasionally on the opposite side, is not uncommon.
- (2) Stab or bullet wounds that penetrate the lung. In such cases the condition is complicated by hæmothorax.
- (3) 'Sucking' wounds of the chest wall.
- (4) Escape of air from a divided bronchus (bronchial fistula) after an operation on the lung.

When a large quantity of air is confined within the pleural cavity the pressure is usually greatly raised, and as high a reading as 20 mm of mercury may be registered. Not only is the lung on the affected side compressed but the mediastinum is displaced towards the sound side, and (when the right side is affected) the direct pressure on the great veins and the auricle may impede the blood flow to the heart.

### Closed Pneumothorax

This form of pneumothorax is usually produced artificially as a therapeutic measure to secure rest for a tuberculous lung, air being introduced into the pleural cavity to cause partial or complete collapse (artificial pneumothorax).

By the introduction of air the intrapleural pressure is modified and the expansibility of the lung is proportionately decreased. If, however, the opposite lung is healthy, complete pulmonary collapse may be tolerated without any ill effects, unless the mediastinal septum is unduly flexible, when the respiratory capacity of the opposite lung may be seriously affected by displacement of the septum. In such cases the intrapleural pressure on the side opposite the pneumothorax may be actually raised, and the expansion of the lung may be so hampered that dyspnoea and cyanosis result.

Air in a closed pneumothorax disappears completely in a few weeks and sometimes in a few days. On this account early experimenters with artificial pneumothorax substituted nitrogen for air in the belief that it would disappear less rapidly. It is now known that, owing to the diffusion of gases between the alveoli and the pleural cavity, the composition of the contents of a pneumothorax, even if pure nitrogen or oxygen has been introduced, soon becomes the same as that of alveolar air. For that reason it is now customary to use air for artificial pneumothorax rather than nitrogen, because of its greater convenience.

It has been calculated that the adult pleural cavity will hold 3 000 to 4 000 c cm. of air. Its rate of absorption is very variable, but, on an average, 80 to 100 c cm are absorbed per diem. The rate of absorption is increased by bodily activity, and is diminished by advanced disease of the lung and by pleurisy, whether past or present.

### Hæmothorax

Hæmothorax the accumulation of blood in the pleural cavity is a common result of severe injury to the chest wall with or without damage to the underlying organs. It may follow fracture of the ribs traversing wounds or surgical operations. When air is present in addition—hæmopneumothorax—it usually signifies a concomitant lung injury. Occasionally hæmothorax occurs spontaneously in a seemingly healthy subject.

Apart from shock, the immediate effects of hæmothorax are blood depletion, irritation of the pleura and collapse or compression of the lung varying according to the bulk of the effusion.

In most situations extravasation of blood is followed by clotting. In the pleura the process is modified by a variety of environmental physical factors. For some days the blood remains liquid due most likely to continuous agitation by the heart beat and lung movements and to dilution of the blood by pleural fluid. It is significant that the hæmoglobin content of the extravasated blood is reduced by as much as 30%, and the fibrinogen content is extremely low. If the hæmothorax persists the fibrinogen content rises so that after a week it may exceed the normal blood level doubtless the result of active pleural exudation. The rise in fibrinogen determines the formation of fibrinous clots often of arborescent and intermeshing character both on the pleural surfaces and as a rusty coagulum at the foot of the hæmothorax. Continued deposition of fibrin may lead to partitioning or loculation within the hæmothorax.

If the blood remains within the pleura organization with fibroblasts occurs within the fibrin exudate and a continuous sheet or envelope of tough fibrous tissue develops on both the lung surface and the parietal pleura. The tough membrane encapsules the lung and delays or prevents its expansion, the thickening of the parietal pleura retards movement and may lead to severe contracture and deformity.

### ACUTE EMPYEMA

Acute inflammation of the pleura is often attended by an effusion of serous or sero-fibrinous fluid into the pleural sac, and when such an effusion becomes purulent the condition is called *empyema*. It is still a common disease despite modern advances in treatment of respiratory infections.

#### Ætiology and Sources of Infection

Infection may reach the pleura by any of three avenues (1) directly from the lung, mediastinum or abdomen, (2) by the blood stream (3) through perforating wounds of the chest wall.

(1) **Direct Infection from the Lung, Mediastinum, or Abdomen** The commonest cause of empyema is spread of infection from a lung which is the seat of pneumonia—either lobar pneumonia or bronchopneumonia. It may occur during the acute stages of the pneumonia (synpneumonic), especially in bronchopneumonia but more often it occurs when the pneumonia is undergoing resolution (metapneumonic).

The micro-organism is usually the same as that of the initial pneumonia. In lobar pneumonia it is generally the pneumococcus, in bronchopneumonia it is sometimes a streptococcus which is usually of a hæmolytic type. Sometimes the two organisms coexist. As the reaction of the pleura differs in many respects in pneumococcal and streptococcal infections, it is important, especially from the point of view of treatment, to differentiate between the two types (see below).

Occasionally empyema follows rupture of an acute lung abscess on the pleural surface, and in such cases the pus is often putrid and contains anaerobic organisms, such as *Cl. Welchii*, spirochaetes, and large fusiform bacilli. In this type of empyema the pleural cavity often contains air (often under tension), derived from the lung (pyopneumothorax). Putrid empyema was formerly a common occurrence after operations for bronchiectasis.

Empyema frequently follows suppuration in the peritoneal cavity. It is most common as a complication of perforated duodenal or gastric ulcer, suppurative appendicitis, or abscess of the liver. It is sometimes preceded by a subphrenic abscess. The avenue of infection in such circumstances is probably the subdiaphragmatic lymph plexus. The right pleural sac is more often involved than the left, and the bacillus coli is the organism commonly present.

In rare cases empyema follows those infections of the mediastinum that arise, for example, from osteomyelitis of the vertebrae, from perforating wounds of the œsophagus, or from cellulitis of the neck. In such cases the infecting organisms are generally streptococci or staphylococci, sometimes accompanied by other bacteria, and the disease takes a rapid course and usually is fatal.

(2) **Infection by the Blood Stream** Empyema of hæmatogenous origin is generally streptococcal or staphylococcal. Usually it is a complication of acute tonsillitis, scarlet fever, puerperal sepsis or pyæmia. Usually there is an intermediate pulmonary lesion such as multiple abscesses at the surface of the lung.

(3) **Infection through Penetrating Wounds** Empyema from direct infection may arise from bullet or stab wounds or after operations on the thoracic viscera. The presence of effused blood in the pleural cavity predisposes to infection.

### Types of Empyema

The pathological changes in the pleura and the lung vary with the organism responsible, and the differences between pneumococcal and streptococcal infection are sufficiently great to warrant separate descriptions.

**Pneumococcal Type** Pneumococcal empyema generally occurs a week or more after the crisis of lobar pneumonia. The Type I organism

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discovery of thick pus on aspiration, for almost certainly by the time that the exudate has changed from its initial sero fibrinous nature to a purulent character the pneumonia will be resolving, the patient's vital capacity will have increased, and pleural adhesions will have formed. In all cases, general and local conditions should determine the appropriate time for, and method of, intervention.

### Effects of Empyema

A large empyema may cause considerable compression of the lung, and may push the heart, great vessels and trachea towards the opposite side.

If the pus is not evacuated, the exudate becomes organized and the pleura greatly thickened, the walls of the empyema cavity may be 25 mm or more in thickness and may become calcified. If the empyema is not drained and if the exudate is large the lung is compressed into a small fibrous mass against the vertebral column, where it is fixed by the thickened pleura, and much deformity of the chest may follow.

The pus of an undrained and active empyema may burrow into the lung, or it may perforate an intercostal space (*empyema necessitatis*). External rupture usually occurs at the front of the chest close to the sternum.

### Special Types of Empyema

**Interlobar Empyema** Occasionally a pleural effusion is confined to one of the pulmonary fissures, especially in the right lung, and when suppuration occurs a circumscribed abscess results. Such an empyema is usually small and may rupture into the pleural cavity, but more often opens into one of the large bronchi, after which its walls become approximated from expansion of the surrounding lung, and spontaneous restoration results. In rare cases an interlobar empyema becomes organized and its capsule calcified.

**Mediastinal Empyema** A purulent pleural effusion may become localized in that portion of the pleural cavity that abuts on the mediastinum, and may simulate a collection of pus in the mediastinum.

**Apical Empyema** In rare instances an empyema may be localized in the apical region of the chest, either in front, behind, or laterally. It possesses no special features except that cardiac pulsation may be transmitted to it, especially when it is situated on the left side.

**Bilateral empyema** sometimes occurs as a complication of broncho pneumonia in children or of influenza in adults. It calls for special consideration in regard to treatment.

**Pyopneumothorax** is most often associated with tuberculosis but may follow rupture of an acute lung abscess into the pleura. The infecting organisms are usually of a virulent type, pleural adhesions are absent or insecure, and not only may the infective process be severe but there is the added embarrassment of tension pneumothorax. Following rupture intrapleurally a pulmonary abscess usually heals although a bronchopulmonary fistula may persist for a time after the empyema has been evacuated.

Tuberculous pyopneumothorax is usually due to breaking down of tuberculous foci at the periphery of the lung or to rupture of the wall of a tuberculous cavity. The condition not infrequently arises during treatment of pulmonary tuberculosis by artificial pneumothorax. Tuberculous empyema is usually preceded by a serous effusion. If the pleural effusion contains large numbers of tubercle bacilli and/or



FIG. 14a. Acute empyema confined to the mediastinal aspect of the right pleural cavity

polymorph leucocytes it can be predicted that the effusion is likely to become purulent. Tuberculous empyema usually undergoes gradual healing if there is no superadded infection and if the disease in the underlying lung resolves. usually, in time the effusion accumulates more slowly and becomes less turbid. *Pari passu* with this process the collapsed lung re-expands and the pleural space may obliterate unaided by surgical means, though, in a few, they may be needed.

#### Rare Forms of Pleural Effusion

Chylous effusion (chylothorax) is uncommon. It may arise from injury to the thoracic duct and pleura in fractures and gun-shot wounds, or from injury during operations on the oesophagus. The fluid tends to accumulate rapidly and may lead to fatal asphyxia. At first it is often



bloodstained, later it is yellowish white and the microscope reveals fat droplets and a variable number of lymphocytes

Pseudo-chylous effusion is the name given to opalescent and milky effusions sometimes associated with malignant diseases of the lung and pleura

Biliary effusion is very rare. It occurs as a complication of suppurative lesions of the liver or the bile ducts, after the establishment of a fistulous communication through the diaphragm

Cholesterol effusion is exceedingly rare. The exact cause is unknown. It is usually preceded by a serous or sero-sanguinous effusion which may be general or localized. The fluid is usually of brownish colour and contains the characteristic crystals of cholesterol. The surface of the pleura may be gritty from the accumulation of cholesterol. It is an occasional complication of a tuberculous effusion

### CHRONIC EMPYEMA

In ordinary circumstances the walls of an empyema cavity are approximated mainly by expansion of the lung and, to a less extent, by ascent of the diaphragm, shrinkage of the chest wall, and deflection of the mediastinal septum. The opposed surfaces of the parietal and pulmonic pleuræ bounding the cavity adhere to each other owing to the sticky character of the effusion that covers them. Organization takes place in this effusion, binding the two pleural layers together and permanently obliterating the cavity. These natural processes of obliteration and healing may be incomplete, and the space persisting between the pulmonic and parietal pleuræ is known as a chronic empyema

**Ætiology.** The chief factors which lead to this chronic state are (a) persistence of infection, and (b) failure of the lung to expand. Either or both of these factors are usually attributable to one or more of the following causes —

(1) Undue delay in the drainage of an acute empyema, particularly one of pneumococcal type, which allows the thickened pleural surfaces to become organized and rigid, and thus prevents re-expansion of the lung

(2) Too early drainage of an acute empyema, particularly one of the streptococcal type, in which absence of adhesions permits complete collapse of the lung

(3) Inadequate drainage through a small or tortuous or improperly placed opening

(4) The presence of portions of dead rib or of foreign bodies, such as a rubber drainage tube

(5) The presence of tuberculosis, abscess or new growth in the lung, or of suppurating cysts in the lung or mediastinum

(6) The presence of a broncho-pleural fistula, which maintains infection and also reduces the inspiratory expansion of the lung

**Morbid Anatomy.** When an empyema cavity fails to heal a sinus usually persists, and pus may escape from it continuously or intermittently. It frequently happens that the wound in the parietes heals

temporarily, and after a variable period reopens and pus escapes again. Healing and discharge may alternate during many months or years, and in such cases the accumulation of pus in the pleural cavity may be attended by fever, and a variable degree of systemic disturbance.

The size and shape of a chronic empyema are very variable. The cavity may be quite small, or it may involve practically the whole side of the thorax. Usually the cavity is in the paravertebral gutter,



FIG. 146. Calcification in the walls of a chronic empyema.

and is large below and tapering towards the apex of the chest. Smaller cavities may communicate with the main chamber like diverticula.

The walls of the cavity, formed by the pulmonic and parietal pleura, are often greatly thickened and tough. If the cavity contains no pus the surfaces may be quite smooth and dry; but when infection remains and there is a collection of pus the pleural surfaces are coated with a purulent exudate of lymph or with soft oedematous granulation tissue. In old-standing cases the exudate may undergo calcification so that the cavity is lined with a calcareous shell (Fig. 146).

Operation offers a favourable opportunity for studying the characters of the tissues surrounding a chronic empyema. The ribs are

usually close together and may *overlap* one another if there have been previous operations they may be fused. The bone varies in density according to the duration of the empyema, in recent cases the periosteum is thick and vascular and the bone less dense, in old standing cases the ribs are atrophic from disuse. The parietal pleura may be three or more centimetres thick and is often oedematous and bleeds freely, in older cases it is extremely dense and unyielding and may be as hard as leather. Areas of calcification (or even of bone) may be present in the thickened membrane. When the diaphragmatic pleura is affected, the diaphragm is usually fixed in an elevated position. When the pericardial pleura is involved, the resulting adhesions may embarrass the action of the heart (pleuropericardial adhesion).

The pulmonic pleura also is thickened, though seldom to such an extent as the parietal and the thick and rigid pleura interferes with the expansion of the lung. A plane of cleavage between the original pleura and the organized exudate may be discovered sometimes easily, usually with difficulty. The lung, though reduced in size is often capable of full expansion if liberated from its adhesions. If the cavity is very large the lung may be reduced to very small size and fixed against the bodies of the vertebrae. In a few cases the lung becomes the site of atelectasis and fibrous induration, and is then incapable of expansion.

If chronic empyema is of recent origin and if infection persists healing may be promoted by adequate drainage and by measures to encourage re expansion of the lung. When the cavity is of old standing mechanical factors are the chief barrier to healing. Obliteration of the cavity may be attempted by stripping the thick pleura from the lung (*decortication*) but if (as is usual) no plane of cleavage is found the rigid outer walls of the cavity may require removal so that the muscles and skin may adhere to the pulmonary wall of the cavity.

**Effects of Chronic Empyema** In young subjects the fibrosis and consequent contraction induced by a chronic empyema are apt to interfere with the development of the thorax and to cause great deformity. The affected side becomes shrunken and immobile, and the intercostal spaces are narrowed, while the diaphragm is elevated and the mediastinum is deviated towards the affected side. As a secondary result an extensive scoliosis may develop.

The existence of a chronic empyema is sometimes compatible with fair health, but often it leads to toxæmia and eventually to anaemia, emaciation and amyloid disease whose recognition should be sought at an early stage by modern methods. As in other thoracic suppurations, an occasional fatal complication is an abscess of the brain.

## DISEASES OF THE LUNG

### MASSIVE COLLAPSE OF THE LUNG—Atelectasis

Collapse of part of a lung or of the whole of it is agencies that exert pressure on it from without, and it them are pleural effusion and pneumothorax. In these

collapse of the lung occurs *passively* in response to the external pressure, and the extent of the pulmonary collapse is, of course, proportionate to the pleural space occupied by the compressing agent, and the lung, though partly collapsed, remains capable of a limited amount of respiratory excursion. But, in the condition known as massive collapse, the lung or part of it, is rendered airless from intrinsic causes, and undergoes *active* collapse for a variable period. The negative intra-pleural pressure, exaggerated by the sudden shrinkage of the lung, maintains the apposition of the lung to the parietes, and to prevent the formation of a vacuum the mediastinal septum is drawn to the affected side. The cause of the pulmonary deflation is absorption of the alveolar air after obstruction of the bronchi of the affected part of the lung. Such collapse is commoner on the right side and most often affects part of or the entire lower lobe of the lung.

Massive collapse is most frequent as a complication following surgical operations, especially those on the abdominal viscera, but it has occurred after fractures of the limbs or injuries to the thorax. It may follow any form of anesthesia, even local. The subjects of this complication are usually strong adults and the greatest number of cases have followed operations on the appendix, and the gall bladder, and those for hernia.

**Mode of Onset and Progress.** In the most obvious cases the onset is sudden—often within forty-eight hours of operation—and gives rise to an alarming crisis evidenced mainly by severe dyspnoea and pain in the chest. Sometimes the symptoms are less dramatic, and in others are so slight that the condition may not be suspected. Often there is premonitory evidence such as flushing of the face, tightness of the chest and cough. The temperature rises suddenly to about  $101^{\circ}$ , and the pulse rate is increased.

During a severe attack the appearance and attitude of the patient are characteristic. There is dyspnoea accompanied by cyanosis. The patient lies on, or inclines towards, the affected side. Cough is slight and sputum is scanty or difficult to expel. The patient may remain in distress for 12 to 36 hours or longer, relief may come abruptly after violent coughing or after a sudden movement. As the attack subsides a considerable quantity of purulent tenacious mucus may be expectorated.

During the attack the affected side of the chest is almost immobile, and is flattened, and the ribs are approximated. Deflection of the heart towards the side of collapse is one of the most characteristic signs. On percussion there is dullness corresponding to the portion of lung collapsed, and the breath sounds and vocal fremitus are diminished. The physical signs may alter from time to time, and tubular breathing and coarse crepitations may be present as the attack terminates.

The collapsed portion of the lung is represented in a radiogram by a uniformly opaque shadow. The mediastinal septum is deviated towards the affected side the ribs are approximated and the diaphragm is elevated. The unaffected side shows abnormal translucency from "compensatory" emphysema (see Fig. 147).

The intrapleural pressure on the affected side is reduced to  $-15$  or  $-20$  mm of mercury, and respiratory movements effect practically no change in the reading

**Causation** There has been much discussion as to the exact cause of massive pulmonary collapse, and many theories to explain its origin have been advanced. Argument has been centred chiefly around the nature and the mode of production of the bronchial obstruction that culminates in atelectasis. The view most widely held and most susceptible of proof, is that the collapse of the lung is due to the obstruction of one or several of the larger bronchi by tenacious exudate such as is likely to accumulate when there is already some degree of bronchial catarrh and respiration is impeded by diminished movement of the



FIG 147 Post operative massive collapse of the lung. A radiogram two days after the onset of massive collapse following operation for perforated gastric ulcer. Note the increased density at the left base and the deviation of the heart and the trachea to that side.

diaphragm and abdominal muscles. The bronchial obstruction is followed by the absorption of most of the alveolar air, and the unsupported vesicles of the lung collapse.

Other theories, not always based on observation, have attributed the bronchial obstruction to reflex spasm of the bronchioles of one region of the lung to oedema of the bronchial mucous membrane and to circulatory changes in part of the lung.

It is not surprising that massive collapse may be associated with or followed by bronchopneumonia or even bronchiectasis. The mechanical obstruction of the chief bronchi favours stagnation of secretions and propagation of infection and the negative pressure within the collapsed lung tends to draw the exudate still more distally within the bronchial passages.

Atelectasis of more gradual onset is common in conjunction with

many diseases of the lung, especially catarrhal infections of the bronchi, foreign bodies, tumours and tuberculous glands at the lung root. The extent of collapse varies according as a main or subsidiary bronchus is occluded. In extreme examples, as when the main stem bronchus is blocked by a carcinoma, the entire lung is affected and becomes shrunken and solidified. More often one or more segments of the bronchial tree are affected and the resulting collapse has a characteristic topographical distribution, easily recognized radiographically. In some instances especially in atelectasis due to pressure of a tumour, one lobe of the lung may be completely collapsed and the other may be emphysematous due to valvular occlusion of its bronchus from extrinsic pressure so that air may enter the lobe freely, but is denied escape (obstructive emphysema).

### POST-OPERATIVE PULMONARY EMBOLISM

Embolism within the pulmonary arteries is still one of the chief anxieties after abdominal operations, and post mortem records prove that it is the immediate cause of death in at least 2% of instances. The underlying causes of this catastrophe have been studied from many angles and considerable advances have been made in our knowledge of its origin, prevention, and treatment.

Pulmonary embolism is commonest in stout and debilitated subjects over the age of forty years. It is most likely to follow operations on the pelvic organs, but it may occur after simple operations for appendicitis, hernia, and even uncomplicated childbirth. It is of much significance that it scarcely ever occurs after operations on the upper part of the body, scarcely ever, those on the thorax.

The time of onset of pulmonary embolism ranges from 48 hours to as long as 6 weeks after operation, but the usual time is about 8-10 days, corresponding often to the time when a convalescent patient begins to resume activity.

Premonitory signs and symptoms are generally absent in pulmonary embolism but detailed study of the course of convalescence suggests that there has been mild transient or outspoken thrombosis in the veins of the lower extremities or the pelvis. Pain and tenderness in the calf muscles, and pain on dorsiflexion of the ankle may be evidence of its occurrence. It is noteworthy that extensive and obvious venous thrombosis, even in subjects of varicose veins, is usually lacking.

The severity of pulmonary embolism depends on the degree of occlusion of the pulmonary artery or its branches. Gross embolism causes sudden death, occlusion of a branch of the pulmonary artery (usually to the lower lobes) may be survived for a considerable time, and a minor embolus gives rise to a hæmorrhagic infarction of a segment of the lung associated with pleuritic pain and hæmoptysis. Non fatal embolism may be repeated on the same side or the opposite.

The post mortem examination of the fatal cases of pulmonary embolism should be carried out with expert and detailed care if every aspect of the condition is to be revealed lest erroneous conclusions be formed. The heart and pulmonary vessels should be examined in

continuity, as occasionally thrombosis may occur primarily in the pulmonary arteries

In most examples of pulmonary embolism the clot is firm, but soft, and usually unorganized. It is either tubular or coiled, and there may be accessory clots alongside it or within the right ventricle or auricle. The trunk of the pulmonary artery, the roots of its two branches or

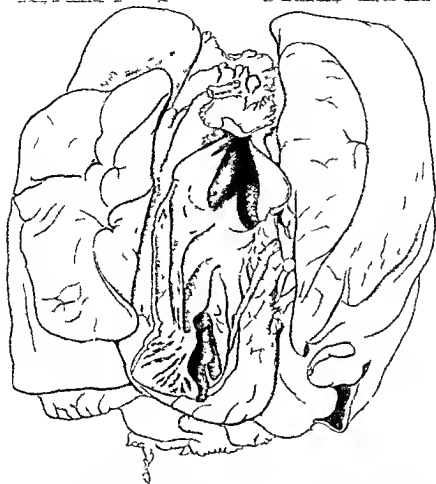


FIG. 148 Pulmonary embolism. Embolism occurred eight days after an operation for ventral hernia in a woman aged sixty-two years, who survived the sudden onset of pain and dyspnea for fifteen minutes. The right iliac vein was the site of thrombosis. Note the coiled embolus in the right ventricle.

the lobar divisions may be blocked. Most interest is attached to the source of origin of the thrombus, and it is in this connexion that accurate accumulated information is inadequate. Obvious thrombophlebitis is seldom evident; the primary thrombosis is of "silent" type and escapes notice. The known sites of origin are "inter alia" the large veins of the thigh and calf muscles, the pelvic veins, the vena cava, and rarely the right auricle. The offending clot may be a mere "tag" or "tail" of the primary thrombotic process.

**Ætiology of Pulmonary Embolism.** Pulmonary embolism is the outcome of venous thrombosis at a peripheral source. The factors which predispose to its occurrence and which favour migration of emboli are of great practical importance. Pulmonary embolism is exceedingly rare except after operations on the abdomen and the lower part of the body and probably curtailment of movement of the abdominal muscles, gaseous distension and prolonged decubitus are responsible for the retarded venous flow which favours intravascular clotting. Aggravating factors are shock, debility, anaemia and constrained posture during and after operation. The time at which thrombosis occurs is not known though its occurrence is most likely when venous stasis is of maximum degree. Once started thrombosis may extend and portions of clot exposed to the active circulation or sudden muscular movements, may be detached into the circulation. Venous stasis is probably by far the most important underlying cause of post-operative thrombophlebitis but there are other contributory factors such as the release of excessive amounts of thromboplastin from trauma at operation, and the creation of Fibrinogen B which promotes intravenous thrombin formation and inhibits the natural formation of fibrin and clot fixation. Indeed detection of large amounts of fibrinogen B in the blood is held to presage intravascular clotting styled the prethrombotic phase.

It is of interest to note that surgical practice in regard to pulmonary embolism has ranged from the boldest to the mildest. Once the Trendelenburg operation of embolectomy was figured in text books and has now given place to anticipatory ligations of peripheral veins. The application of anticoagulant drugs (heparin etc.) and forced post-operative activity is the present compromise.

**Primary Thrombosis of the Pulmonary Arteries.** There is evidence that thrombosis may occur primarily in the pulmonary arteries especially in the lower lobe vessels as a result of vascular stasis. It is believed that its occurrence is likely when there is an excess of fibrinogen B present in the blood. For the same reason a comparatively small non-lethal embolus may be followed by extensive thrombosis peripherally and may determine a fatal outcome.

### FAT EMBOLISM

Emboli of fat may lodge in the lung and sometimes the brain and other organs and their effects may be fatal. This form of embolism sometimes follows fractures of long bones in adults and develops some three or more days after the accident. Less often it follows operations on bones (especially if they are rarefied) manipulation of joints or trivial injuries. There are no reliable methods of estimating or assessing the presence, progress or outcome of fat embolism.

Fat emboli probably come from the site of injury but the local condition which favours their entry into the circulation is not understood. There is some unconfirmed experimental evidence that the blood plasma fat may be precipitated in the capillaries of the lung under certain conditions especially if ether anaesthesia has disturbed the



normal processes of emulsification of fat. There is, too, a suggestion that some of the effects of fat embolism are due to hydrolysis by lipase, and that the fatty acids and soaps produced are toxic.

There are two types of fat embolism and they may be combined—the *pulmonic* (usually survived), in which the effects are due to widespread embolism in the terminal vessels, and the *systemic or cerebral*, in which emboli lodge in different viscera (usually harmlessly) and the brain, where they commonly lead to fatal ischæmic effects.

It is assumed that fat emboli reach the general circulation as a result of the increased circulatory tension in the lungs following upon obstruction of its vessels, or in some instances *via* a patent *foramen ovale*.

In fatal cases the appearance of the affected organs is characteristic. In the lungs there are areas of congestion and œdema and hæmorrhages beneath the pleura, and specific stains outline the fat droplets within the alveolar capillaries.<sup>1</sup> In the brain the emboli lodge chiefly in the grey matter and produce in its terminal vessels multiple foci of hæmorrhagic extravasation, likened to sprinkling of cayenne pepper.

More widespread embolism may be suggested by the discovery of fat droplets in the urine, though the kidney tubules are apparently undamaged.

## AIR EMBOLISM

Air seldom enters a vein, but it may do so during operations in the neck or in the axilla or after stab wounds, and it has occurred during intravenous administration of fluids.

Entry of air into a wounded vein depends on the negative intravenous pressure which is caused by the suction power of the thorax and to a less extent by that of the heart. It is most likely to occur where collapse of a vein is hindered by stiffening of its wall due to disease or by adhesion to dense fasciæ. The entrance of air is recognized by a hissing sound in the wound and this is followed by a churning sound in the chest caused by the air in the heart.

Air embolism may occur at operations without apparent ill effect, for small amounts of air are held up in the pulmonary capillaries and are dissolved in the blood. Nevertheless, air embolism sometimes terminates fatally and at autopsy the right side of the heart is full of frothy blood. One or both lungs may have a bloodless appearance.

Cerebral air embolism sometimes occurs during paracentesis of the chest, and especially during the induction of pneumothorax. Formerly the condition was confused with "pleural shock," which it resembles. The embolism is due to the entry of air into one of the pulmonary veins as a result of puncture of the lung. The air may reach the pulmonary veins either through the needle employed or from the alveoli of the lungs. It should be borne in mind that the pressure in the pulmonary veins is a negative one and that the air in the alveoli is at a slight positive pressure and may therefore be aspirated readily.

<sup>1</sup> Emboli of fat can be demonstrated within the lungs in about 14% of subjects after death.

into a wounded vessel. The aspirated air passes through the left side of the heart to the systemic vessels and a large proportion of it is directed to the carotid arteries and thence to the brain and may cause loss of consciousness blindness paralysis or even death.

Experimental observations suggest that quantities of air over 20 c c introduced into the pulmonary veins may have a lethal effect.

## SUPPURATION IN THE LUNG

### Bronchiectasis

Many cases of bronchiectasis date back to childhood and owe their origin to bronchopneumonia or bronchitis following measles or whooping-cough. When the disease begins in adult life it is usually due to bronchopneumonia from any sort of origin. Either in children or adults bronchiectasis may follow the aspiration of a foreign body or other infective material into the lung. In a considerable number of cases no definite antecedent ætiological factor except an acute respiratory infection can be discovered.

When bronchiectasis follows acute respiratory infection the changes in the lung can be traced to an acute interstitial inflammation going on to necrosis and suppuration, which destroys the bronchial wall (including the muscle elastic tissue and cartilage) invades adjacent alveoli and creates a cavity alongside the bronchus and in communication with it. The cavity may be cylindrical or saccular according to the extent of the destruction. In the healing process the walls of the cavities are converted into granulation tissue, which later becomes fibrous tissue and are lined with bronchial epithelium derived from proliferation of such islets of mucosa as have not perished during the acute inflammatory process. The epithelium is of a varied type—cubical, stratified or squamous.

In many cases of bronchiectasis (the so-called idiopathic) the pathogenesis is more insidious and probably the outcome of atelectasis resulting from bronchial obstruction by chronic inflammatory exudate or tuberculous hilar glands. The atelectasis is associated with an increased negative pressure in the collapsed lung which if sustained, brings about dilatation of the more slender portions of the bronchial tree distal to the obstruction. Such anatomical possibilities have been supported by clinical and experimental observation and it has been shown that the bronchial dilatation may disappear if the occlusion is relieved at an early stage and if free ventilation of the affected segments is encouraged.

In a bronchiectatic lung there is always a variable amount of interstitial fibrosis. It is greatest around the bronchi, but it is present also in the walls of the alveoli and may sometimes extend to the surface of the lung. The fibrosis stiffens the walls of the bronchiectatic cavities and tends to keep them open and hence the stagnation of secretions and persistence of infection which are such characteristic features of bronchiectasis. The destruction of muscle fibres and loss of the ciliated epithelium probably play a minor part in the retention of secretions.

In all cases it is the severity of the superadded infection which determines the clinical manifestations of the disease. Thus in some it is latent (*dry bronchiectasis*), in others there is repeated (though rarely fatal) hæmoptysis, and when there is gross infection, copious, often foul smelling, sputum.

Bronchiectasis may be scattered throughout the whole lung, but more often is confined to a part or the whole of the arborescences of the lower lobe bronchus, with in addition sometimes the lingula portion of the lobe above on the left side. Occasionally the disease is bilateral from the onset, or it may become so later. On account of the diffuse fibrous infiltration, chronic inflammation, and the loss of elasticity, the lung is smaller and more solid than normally, and its power of expansion is greatly diminished. Pleural adhesions are often present, especially at the base of the lung but sometimes they are absent even in severe cases. The lymph glands at the hilum of the affected lobe are usually enlarged, sometimes to a very considerable size, and may hamper surgical operations.

Bronchiectasis may be consistent with a state of moderate health, but in many instances it is responsible for dyspnoea, cyanosis and chronic toxæmia. Exacerbations of the pulmonary infection may occur from time to time and may lead to a fatal issue. In a number of cases a metastatic cerebral abscess is responsible for death, sometimes the abscess is single, but quite frequently there are multiple abscesses in different parts of the brain.

### *Abscess of the Lung*

A lung abscess differs from bronchiectasis in that it begins in the parenchyma of the lung (pneumonitis) and involves the bronchi only secondarily. The mode of origin and the ultimate behaviour of a lung abscess are very varied, and a satisfactory classification of the various types either on a bacteriological or anatomical basis is not possible. There are, however, familiar and well recognized types resulting from local or distant infective processes. A description of the common varieties follows.

(1) *Putrid Lung Abscess (Gangrenous Abscess)* This is by far the commonest and most urgent form of lung abscess. Anaerobic bacteria are responsible for the intense inflammatory and destructive effects which characterize it. The usual source of infection is the oropharynx and particularly the gums and tonsillar crypts. The infective material reaches the finer bronchi by aspiration (so called bronchial embolism), and the particular segment of the lung affected is probably conditioned by posture during sleep, narcosis, anaesthesia, etc. Dental extractions, tonsil removal and other operations on the upper respiratory passages are responsible for a proportion of cases.

In this variety of abscess any segment of the lung may be affected, but by far the commonest sites are the subapical segment of the upper lobe bronchus, and the apical segment of the lower lobe. The inflammatory process begins peripherally with an intense pneumonic reaction in which softening and necrosis finally occur. The course of the inflammatory process is very variable, but usually after 10-14 days the

abscess burrows into a bronchus and large quantities of evil-odoured pus are expectorated. At this stage the abscess (on the average the size of a tangerine orange), has soft and necrotic walls, and is situated near the surface of the lung; one or more inflamed bronchi communicate with it. The outer wall is quite thin and avascular and is usually lightly adherent to the parietal pleura. Natural and complete healing occurs in a very small proportion, and its occurrence can not be predicted in anyone. Failure to heal is doubtless due to defective drainage, and the persisting distension of the abscess cavity by imprisoned air. When the abscess becomes chronic the surrounding lung becomes stiff and consolidated and the seat of bronchiectasis. The epithelium, often of squamous type, regenerates within the wall of the cavity at an early date.

In some instances a lung abscess ruptures into the pleural cavity. This accident, though it may have grave consequences (especially from shock and tension pneumothorax), usually results in healing of the abscess after the empyema has been treated. In the treatment of lung abscess by drainage there may occasionally be sufficient adhesion of the outer wall of the abscess to the parietal pleura to provide a safe barrier against contamination of the pleural cavity.

The common variety of abscess in the upper lobe of the lung presents on the surface on the axillary face of the lung immediately above the interlobar fissure. An abscess of the lower lobe most often involves the apical portion and reaches the surface behind, usually about the level of the seventh rib: in rare instances it presents on the mediastinal aspect of the lung.

Sometimes suppuration in the lung is chronic from the outset and extends gradually over a period of many months to involve almost every segment of the lung. The lung, which is extensively consolidated and oedematous is the seat of multiple abscess cavities containing foetid pus and yellow sloughs. The disease is described under the title of "spreading suppurative pneumonitis," and it is not often survived.

(2) *Non-Putrid Solitary Abscess.* This type is much less common. It is caused by aerobic streptococci, etc., which reach the lung by aspiration. It may follow any variety of pneumonia. The course of the disease is much less acute than in gangrenous abscess, so much so that the abscess becomes encapsuled in inflammatory fibrous tissue and may simulate tuberculosis or carcinoma. The outlook is more favourable than in other varieties of abscess. In many instances the abscess is responsible for recurring hæmoptysis which may be an indication for removal of the affected segment of the lung.

(3) *Staphylococcal Abscess.* An abscess of this origin may develop in the lung in the course of staphylococcal pneumonia or as a late complication of influenzal pneumonia. It may be associated with similar infection elsewhere, e.g., in joints. A staphylococcal abscess frequently involves the pleura secondarily. The disease though often fatal is sometimes survived.

(4) *Following Aspiration of Foreign Bodies.* Foreign bodies aspirated into the bronchi may after a variable interval lead to suppuration, especially bodies such as peas, nuts, etc., which undergo expansion and

harbour infective material. Relatively sterile objects such as fragments of metal or beads may remain in a bronchus for months or even years without causing more than slight disturbance.

On account of the greater width of the right bronchus, an aspiration abscess is commoner in the right lung, and is most frequent in the lower lobe because of the more vertical direction of the hyperarterial bronchus. When a foreign body becomes impacted in a bronchus the mucous membrane surrounding it becomes swollen, so that obstruction of the bronchus may become complete. The lung beyond it becomes atelectatic. Secretion of mucus from the bronchus is increased at the site of impaction, and ulceration and infection generally occur. The infection spreads through the bronchi into the lung parenchyma, and may give rise to single or multiple abscesses. The abscess is generally multilocular and has the combined features of bronchiectasis and a chronic lung abscess.

(5) *Pyæmic*. In infected surgical wounds, septic thrombophlebitis, acute osteomyelitis, etc., infected emboli may be carried by the veins to the lungs, where they give rise to septic infarcts and abscesses. The abscesses are usually small and multiple and situated at the periphery of the lungs. The disease is likely to be fatal.

(6) *Associated with Tumours, etc.* The ulcerated surface of a carcinoma is very liable to infection. Suppuration, aggravated by necrosis of the tumour, may result in a large abscess, and render treatment impossible.

Less common causes of a lung abscess are (a) lodgment of missiles or of infective material conveyed by them, (b) extension of a subphrenic abscess, and (c) superadded infection of a congenital or hydatid cyst in the lung.

*Pathological Sequelæ of a Lung Abscess*. One common sequelæ of a pulmonary abscess is *cerebral abscess* (most often in the left hemisphere), due probably to an embolus formed by the dislodgment of a thrombus from one of the pulmonary veins. This catastrophe can occur during either the acute or the chronic stage of the abscess, and occasionally follows operative interference. *Hæmorrhage* may result from ulceration into one of the pulmonary vessels in the wall of the lung abscess and be fatal. *Amyloid disease* is a sequel of long standing lung abscess.

## SURGICAL ASPECTS OF PULMONARY TUBERCULOSIS

In early life the lungs are the commonest site of primary tuberculous infection, and the initial focus is usually insignificant and heals in due time. The lymph glands at the hilum of the lung may harbour infection for a prolonged period and may occasionally be responsible for propagation of disease either within the lung or in distant sites such as the meninges and bones and joints. Enlarged hilar glands may impinge upon, or invade the main bronchi and lead to atelectasis and finally bronchiectasis.

In adult life tuberculosis of the lungs may be due to relapse of

earlier disease, but it is more often acquired from exposure to a fresh and virulent infection.

Broadly there are two main pathological types of pulmonary tuberculosis—the acute or sub-acute exudative, or infiltrating variety with a tendency to caseation and cavity formation, with only slight tendency to repair by fibrosis—and the productive more chronic fibroplastic type usually associated with pronounced fibrosis, shrinkage and cavities large or small. In favourable circumstances the first type

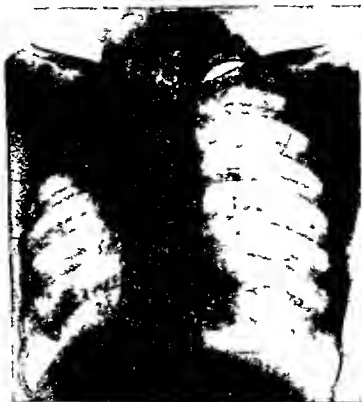


FIG. 149. Radiogram of chronic fibroid phthisis of the right lung in a female aged twenty-four years. The trachea and the heart are deflected towards the diseased side.

may assume finally a fibrocavernous form. The condition of the pleura is important in regard to the feasibility of some forms of surgical treatment, thus if the surfaces have been the seat of pleurisy there will be diffuse or localized adhesion which will be a barrier to effective artificial pneumothorax unless division of the adhesions is possible.

Cavities in the lung are commonest in the upper lobe, but they are also common in the lower lobe especially its apical portion. Persistence of a cavity is one of the most compelling and urgent reasons for adopting surgical treatment. Persistence of a cavity may be due mainly to stiffness and loss of elasticity of its walls and adhesion to the chest wall. Many cavities, however, remain patent due to continuous

distension of the walls by air trapped within the lumen due to some form (often valvular) of bronchial obstruction—*inflation or tension cavity*. Variation in size of the cavity from time to time is common, and it may reach giant size, even in spite of active treatment.

For the surgical treatment of pulmonary tuberculosis the various methods, either singly or combined, are designed to provide rest or immobilization of the diseased lung and to secure closure of cavities within it. The methods are known collectively as "collapse therapy", they are applicable at some time, in almost every grade of the disease, even when both lungs are affected, provided the disease is not extremely acute or too advanced. The choice of procedure depends on the pathological type of disease. In very acute tuberculosis there is a time to act and a time to refrain, thus artificial pneumothorax may have to be deferred because it is likely to result in an acute effusion or empyema. When the disease has been rendered less acute, say by phrenicectomy combined with pneumoperitoneum, the intrapleural collapse can be adopted.

When pulmonary tuberculosis is more chronic (and not of the ulcerative tracheo-bronchitis type), and the lung is the seat of cavities adherent to the chest wall, the lesser measures are insufficient, it is then that some form of thoracoplasty and mobilization of the comparatively derelict lung is required to effect healing of the disease.

Within recent times resection of a lobe of the lung or even the entire lung has been practiced. Such a step would seem to offer an ideal solution on pathological grounds, unfortunately in a high proportion of instances active disease in the bronchus may be responsible for ulceration and fistula formation with empyema, or for extension of infection to the opposite lung. These complications have to a considerable extent been overcome by the use of the antibiotic streptomycin.

## CONGENITAL CYSTIC DISEASE OF THE LUNG

This condition has attracted increasing interest during recent years, no doubt on account of its frequent discovery on radiographic examination of the lungs. The disease assumes two main forms: (1) a solitary or multiple large cysts, containing fluid or air, and (2) diffuse cystic disease.

The first variety has usually been met with in childhood. The cyst may attain an enormous size and fill the entire pleural sac of one side (the so called balloon cyst). Such a cyst is at first probably of small size and may contain fluid whose escape into a bronchus allows a gradual air distension of its walls so that finally the healthy lung tissue is condensed around it. In the same way multiple cysts may evacuate their contents and become inflated with air, and either form multiple air-containing cysts or, if the dividing walls rupture, a single trabeculated cyst. The lining membrane is usually columnar or cubical epithelium, and the walls contain unstriped muscle, elastic and fibrous tissue and sometimes cartilage. The appearances may be profoundly altered by infection.

A large cyst when uncomplicated may cause only slight symptoms,

such as cyanosis and dyspnoea. But if the air pressure within the cyst becomes excessive (due to a valvular communication with a bronchus) severe respiratory distress or fatal asphyxia may result. In a number of instances rupture of the cyst into the pleural cavity occurs.

Diffuse cystic disease is more common. It may involve a part or the entire lung and is often bilateral. The cysts may be mere clefts but are more often rounded and vary in size from a pea to larger than a golf ball. Many of the cysts communicate with the finer bronchi. The bronchi are not dilated. In an X-ray film the appearance is very characteristic and merits the title of "honey-comb" or "soap-bubble" lung. Superadded infection is common and creates features comparable clinically to bronchiectasis.

The developmental nature of cystic disease of the lung is suggested by its occurrence in infancy and by the epithelial character of the lining membrane of the cysts. It is assumed that in most cases the cysts are developed as diverticula from the smaller bronchi or from the atrial sacs.

Attempts have been made to establish a relationship between cystic disease and bronchiectasis, but the pathological evidence suggests they are independent entities although the condition of bronchiectasis found in infancy may represent a developmental abnormality allied in cystic disease.

Sometimes as a result of inflammatory stenosis of a small bronchus overdistension of a lobule of lung occurs with escape of air into the interstitial tissues of the lung with the result that an enormous cyst develops (bulbous emphysematous cyst). The cyst develops gradually but as the air within it is under increasing tension it may lead to injurious compression of the adjacent lung tissue and if bilateral final asphyxia.

## TUMOURS OF THE LUNG

Simple tumours of the lung are rare. Myoma, fibroma, chondroma, hamartoma and angioma (see p. 231) are well known though except in the last their pathological effects are few and unimportant.

A simple adenoma commonly occurs in one of the main bronchi and may reach a large size. It is commonest in the lower lobe of the lung. It may be responsible for hæmoptysis, atelectasis or bronchiectasis with suppuration (see Fig. 150). It affects men and women equally and occurs at an earlier age (twenty five to forty years) than lung cancer. It shows no tendency to become malignant.

A bronchial adenoma is sometimes pedunculated and is then accessible to removal from within the bronchus. Generally the tumour, which is tough and firm projects into the bronchus and its deeper part expands into the adjacent lung the resulting tumour assuming an hour glass form.

Microscopically a bronchial adenoma shows considerable individual variation in structure. Some show a glandular pattern with tubules and acini. In others there is less differentiation and the cells are in solid acini or irregular masses. The cells are, however, uniform in size and are cuboidal with a large nucleus and scanty cytoplasm.



A bronchial adenoma originates from the secretory ducts of the bronchial mucous glands. Its histological variations are very similar in form and nature to those present in salivary gland tumours and the two types of tumour are held to be akin in origin and behaviour.

### Primary Cancer of the Lung

Statistics based on post mortem records suggest that the incidence of cancer of the lung has increased during the past ten or fifteen years and that the increase is a real one and is independent of improvements in clinical and pathological diagnosis. The cause of the increase has not been fully explained nor accounted for.

Many substances have been suggested as predisposing factors in the development of lung cancer, such as silica, petrol fumes, tar from road dust, etc., but proof is lacking that they are responsible. The only known association between exposure to dust and the development of bronchial carcinoma is that of the Schneeberg miners, and in them the radioactive properties of the dust are now held responsible. By some, chronic bacterial infections are regarded as a potential predisposing cause, probably as a result of the epithelial metaplasia to which they may give rise in the bronchi. Active tuberculosis and carcinoma may coexist in the lung, but the occurrence is purely accidental.

Cancer of the lung occurs most often between the ages of forty and sixty years, and is much more common in men than women, the relative incidence is as high as 15 : 1.

**Morbid Anatomy and Histology** In the majority of cases cancer in the lung begins in the mucous membrane of the main or secondary bronchi and less often more peripherally. The new growth may start in the cylindrical epithelium of the bronchial mucosa or in the basal epithelium. The histological appearances are very diverse, and variations within individual tumours are not uncommon. The follow-



FIG 150 Adenoma of the bronchus. The growth has obstructed the lower lobe bronchus which in consequence is greatly dilated.

ing are the common types: (1) columnar-cell carcinoma, (2) "oat-cell" carcinoma, (3) squamous-cell carcinoma. Tumours of the first type are composed of columnar cells, which are differentiated to a moderate degree and are arranged, for the most part, in an irregular acinar or papillary formation. Tumours of the second, the commonest type—the "oat-cell" carcinoma—are composed of undifferentiated cells of small size, rounded or of oat seed shape, with deep-staining nuclei and scanty cytoplasm. The majority of the cells are arranged irregularly, with a very scanty fibrous tissue stroma and little tendency towards glandular structure. Tumours of this type were regarded formerly as mediastinal sarcoma, but careful examination generally affords evidence of an epithelial origin. Tumours of the third type are composed mainly of irregularly arranged squamous cells, and to some

extent they resemble squamous-cell carcinoma in other situations, though cell nests or keratinization are seldom highly developed.

The rate of growth and the degree of malignancy of bronchial carcinoma are very variable. In some it may be four or five years before the tumour attains the size of a tangerine orange, while in others, and especially in undifferentiated tumour in young subjects, it may assume great bulk in a few

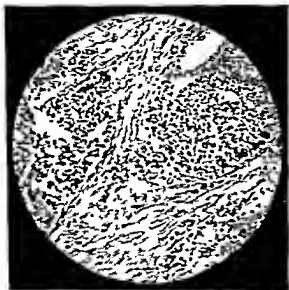


FIG 151 Carcinoma of bronchus of "oat-cell" type  
X 150.

months. When a group of cases is analysed it is found that, when first seen, removal of the tumour is possible in about 15% of instances. Recurrence of the carcinoma either locally or elsewhere is common (40%) within two years of its removal.

A bronchial carcinoma may begin anywhere in the bronchial tree, and probably even in the aveoli (*alveolar carcinoma*); but the commonest point of origin is at or about the point where the main bronchus gives off its branches. It usually spreads both up and down the bronchial wall and also round it and may finally occlude the lumen of the bronchus. When examined by bronchoscopy or at autopsy the growth is often small, greyish white, granular and slightly nodular on the surface. It may be pedunculated and may occlude the lumen of the bronchus. It may spread in the submucosa over a considerable area without ulceration, and it may extend directly to the trachea or even to the opposite bronchus. The most important effect of a bronchial carcinoma

is production of stenosis of the larger bronchi and therefore atelectasis and infection are common secondary results

A bronchial carcinoma tends to infiltrate the parenchyma of the lung till a lobe or even the entire lung may be converted into a solid mass of firm texture and yellowish white colour. Degeneration within the tumour, sometimes attended by suppuration, is a common event. Sometimes spread by the peribronchial lymph vessels is an outstanding feature, and may lead to extensive involvement of the pleura, often



FIG. 132. Bronchial carcinoma. The disease involves the stem bronchi and invades the lung parenchyma.

with a large effusion of clear or sanious fluid due to widespread lymph vascular obstruction. The tracheo bronchial lymph glands and the hilum of the lung are invaded at an early stage, and it sometimes happens that the bronchial growth remains very small and localized, while the secondary growths are large and give rise to pressure on large vessels, and on the trachea. Such secondary growths may be mistaken for mediastinal sarcoma. Rarely the lymph glands at the root of the neck may be infiltrated, especially in carcinoma of the upper lobe of the lung. Occasionally a small bronchial tumour leads to atelectasis so that the

lung is no larger than a fist and the pleural cavity becomes the seat of a very large effusion.

In a few instances a carcinoma begins in a fine or tertiary bronchus and tends to grow peripherally rather than towards the hilum. This type often assumes and maintains a spherical form in the substance of the lung. Its malignancy is held to be as great or even greater than that of tumours at the hilum.

The pathological effects of a bronchial carcinoma may be very few, but in about 25% secondary bronchiectasis occurs. Ulceration of the surface of the growth leads to excessive mucoid or sanious discharge, and sometimes tumour cells can be detected in the sputum by special staining methods.

In rare instances a bronchial carcinoma is associated with widespread arthritic changes and gross clubbing of the fingers as well as deposition of new bone on the shafts of the principal bones. Equally remarkable is the prompt disappearance of the skeletal changes after removal of the tumour.

Apart from the neighbouring lymph glands the liver (30%) is the commonest site of secondary growths. Metastases are common also in the kidneys (15.9%), the suprarenal glands (9.7%) and the brain (9.5%) and the skin. They are common also in bones (10%) especially in the ribs, vertebrae and long bones. A cerebral metastasis may give rise to confusion in diagnosis and errors in treatment if the primary growth is symptomless.

In the majority of cases the onset of signs or symptoms is very insidious and the tumour is often far advanced before they develop. The following are the common ways in which the disease may manifest itself: (1) by hæmoptysis and cough, (2) by pleurisy, with or without effusion, (3) by pulmonary suppuration, (4) by increasing debility, dyspnoea, and emaciation.

## DISEASES OF THE MEDIASTINUM

### Acute Septic Mediastinitis

The areolar tissue of the mediastinal septum is of loose texture, and consequently infective processes tend to spread widely in it and, as it is richly supplied with lymph vessels, toxic absorption is on a severe scale.

Acute mediastinitis is rare but when it occurs takes the form of diffuse cellulitis and the anterior mediastinum is most commonly affected. The cellulitis may on occasions result in the formation of an abscess but its effects may be lethal before suppuration begins.

Mediastinitis may arise (1) as a complication of cellulitis of the neck, e.g., Ludwig's angina, (2) following operations on the larynx, pharynx, trachea or œsophagus, (3) as a result of perforation of the pharynx or œsophagus by a foreign body, (4) from leakage of infection from an ulcerating carcinoma of the pharynx or œsophagus, and (5) rarely, secondary to osteomyelitis of a thoracic vertebra.

In mediastinitis, the tissues are very swollen, cedematous and con-

gested Areas of necrotic fat, often of a greenish colour, are present, and there may be small abscesses scattered through the inflamed tissues When perforation of a hollow viscus has been responsible for the infection, gas may infiltrate the inflamed tissues, which are then extremely malodorous The lymph glands are enlarged and sometimes softened, and the fibrous pericardium may share in the inflammation

When an abscess forms in the anterior mediastinum it may extend upwards and reach the root of the neck at the suprasternal notch, or accompany the subclavian vessels into the posterior triangle, or burrow through an intercostal space at the margin of the sternum An abscess in the superior and posterior mediastina may rupture into the trachea, œsophagus or pleural cavity

*Emphysema of the mediastinum* is a rare sequel of crushing injuries of the thorax The air may escape from the trachea, the bronchi or the lungs At each inspiration more and more air is forced into the mediastinum, and it may finally compress the large veins, especially those at the lung root

Nowadays mediastinal emphysema is sometimes witnessed as a complication of artificial pneumoperitoneum employed for the treatment of pulmonary tuberculosis The air probably escapes from the abdomen alongside the œsophagus, not only may it permeate the mediastinum, but it may extend upwards as far as the base of the skull

### Cysts of the Mediastinum

Cysts of the mediastinum are comparatively rare, but they are of importance on account of the injurious pressure they may cause

The commonest are dermoid and teratomatous cysts generically they are alike They usually begin in the anterior and the superior mediastinum behind the manubrium (retrosternal), in close relation to the great vessels and pericardium Commonly, as the cyst grows, it bulges towards the pleural cavity on one or both sides (mediastino thoracic), or it may reach the root of the neck (mediastino cervical) The origin of the cyst is probably not the same in all cases It is believed (though not proved) that a mediastinal dermoid arises from the caudad displacement of remnants of the third and fourth branchial arches Less often it may arise from inclusion of the epidermis, for defects of the sternum may coexist

In structure a mediastinal dermoid does not differ from those elsewhere It may be entirely cystic or in parts solid Cartilage, sebaceous material, fat, hair, and teeth are common constituents of the tumour

Dermoid and teratomatous cysts vary in size from a golf ball to a foetal head Their growth is slow, and since the cyst extends laterally it acquires a covering of pleura, and it may insinuate itself between the lobes of a lung and thus simulate an intrapulmonary tumour

Mediastinal cysts are very liable to infection, especially after acute illnesses Suppuration causes a rapid increase in its size, and the cyst may perforate the trachea or bronchi, with the result that sebaceous material or hairs are expectorated Empyema may occur and the pus may penetrate the chest wall Inflammation in the cyst renders it adherent to the lung pleura and large vessels, and adds

to the difficulty of its removal. Malignant degeneration of a teratoma and dermoid is unusual.

A much rarer cyst of the mediastinum is the bronchogenic or tracheo-bronchial cyst. It is usually in contact with the trachea or main bronchi and may reach considerable size. The cyst wall differs from that of a dermoid in that it is very thin and lacks hair forming epithelium and sebaceous glands. The epithelium is of a

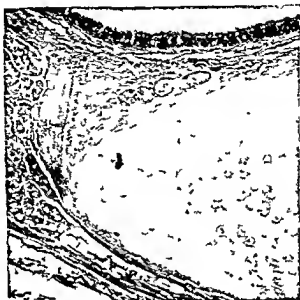


FIG. 153 Tracheo-bronchial cyst. The cyst is lined by ciliated epithelium. Its walls contain areas of cartilage.

cylindrical type, and may be ciliated. Numerous glands and bundles of plain muscle fibres or cartilage may lie deep to the epithelium.

Such a cyst is of vestigial origin, from extrusions of the developing trachea or bronchi.

**Gastrogenic Cysts.** A cyst lined by gastric epithelium with mucous glands occasionally occurs in the mediastinum in early life. It is of particular interest in that the mucous membrane may be the seat of peptic ulceration, and hæmorrhage or even perforation may occur with fatal result.

#### Primary Tumours of the Mediastinum

Malignant tumours of the mediastinum include thymoma (p. 358), lymphosarcoma and neuroblastoma.

Simple tumours include lipoma, fibroma, chondroma, and gangliocœuroma.

Rarely a mediastinal tumour extends through an intervertebral foramen into the spinal canal, assuming an hour-glass shape, similarly a tumour arising within the spinal canal may extend into the mediastinum. Hæmorrhage or degeneration within the spinal portion may result in paraplegia.

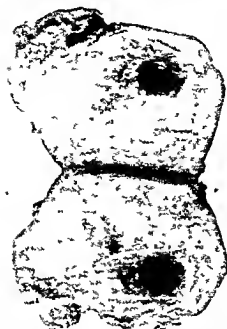


FIG 154 Ganglioneuroma of the mediastinum. The tumour has been split. Note the area of hæmorrhage and multiple foci of calcification.



FIG 155 Radiogram of a ganglioneuroma of the mediastinum which extended into the right side of the chest. The tumour occurred in a female nine years of age, and had caused dyspnoea, hæmoptysis, and paroxysmal coughing.

Lastly there is the fairly common superior sulcus tumour. Under this title is described a localized tumour which arises at the thoracic inlet in front of the first and second ribs and the transverse processes of the respective vertebrae. The tumour is usually sharply defined and spherical and when first observed is seldom larger than a golf ball. It develops at the pleural surface of the lung apex and, as it infiltrates, causes erosion of the ribs and vertebrae and involves the brachial plexus and the sympathetic trunk, with the result that intractable pain and nerve palsies (e.g., Horner's syndrome) are prominent effects.

The tumour is hard and fixed and of grey or yellow colour. The tumour is a primary carcinoma of the lung originating at the apex immediately subjacent to the pleura. In a few examples it is secondary to an insignificant primary one at the lung root. Most often the tumour is of squamoid pattern.

**Pathological Effects of Mediastinal Tumours.** The effects of a mediastinal tumour are mainly due to pressure on neighbouring structures, although in the case of cystic tumours infection may lead to additional features. It is unusual for any disturbance to be noticeable before the age of puberty and symptoms are sometimes deferred until the third or fourth decade. Pressure on the trachea is by far the most important effect. It tends to appear after some respiratory infection, and results in cough and often in dyspnoea or stridor. In a few cases haemoptysis occurs.

Pressure on the large venous trunks at the thoracic inlet may lead to dilatation of the superficial veins of the thorax or in the neck. Cyanosis may be present at a later stage. Pressure on the intercostal nerves may lead to pain or hyperaesthesia, and there may be pupillary changes from pressure on the sympathetic nerves. When large, the tumour may cause localized bulging of the chest wall.

### Intrathoracic Goitre

Any large goitre may have a prolongation of its inferior extremity behind the sternum into the mediastinum. Such extension is favoured by gravity and the suction of inspiration. The resistance offered above and in front by the infrahyoid muscles makes this line of descent the path of least resistance.

In a true intrathoracic goitre however there is no obvious swelling of the thyroid gland in the neck and the thyroid enlargement is entirely within the thoracic cavity.

An intrathoracic goitre is due most often to a colloid adenoma attached to the inferior extremity of the gland, especially on the left side. Rarely the condition is bilateral. The adenoma may be soft or hard but frequently it is partly or wholly cystic, and calcification sometimes occurs in the wall of the cyst. The tumour retains its investment of pretracheal fascia, and its arterial supply resembles that of a cervical goitre and comes from the neck. In many cases the intrathoracic goitre is connected with the parent gland by an isthmus of thyroid tissue but in old-standing cases the connexion may be fibrous.



As the goitre is enclosed in the pretracheal fascia it moves with the rest of the thyroid gland on deglutition. In the superior mediastinum an intrathoracic goitre rests on the parietal pleure of one or both sides which form a bed for it. The innominate veins are situated deep to the tumour and may be displaced and compressed by it. Hyperthyroidism in association with an intrathoracic goitre is extremely rare.

*The Effects of an Intrathoracic Goitre* (1) On the trachea



FIG. 156. Intrathoracic goitre. The trachea was displaced forwards. Stridor and dysphagia were the chief symptoms. The tumour was completely solid.

One of the most important effects produced by an intrathoracic goitre is compression and deviation of the trachea. The trachea becomes stretched over the anterior or lateral surface of the tumour, and as a result its lumen is often reduced to a very narrow channel. The tracheal displacement may be confirmed by inspecting or palpating the neck, and the larynx may participate in the deviation. A radiogram demonstrates the displacement and deformity. Cough, stridor and dyspnoea are the usual results.

(2) On the large vessels of the thoracic inlet. Obstruction to the venous return from the neck and upper limbs is manifest by engorge

ment of the superficial vessels of the neck and front of the thorax. It is responsible for profuse bleeding when operation is undertaken. Sometimes the face and lips and the upper limbs show a trace of cyanosis. Œdema of the upper limbs has been observed. The large arteries are seldom compressed.

(8) On the Recurrent Laryngeal Nerve. Occasionally one of the recurrent laryngeal nerves, especially the left, may show some degree of paralysis.

(4) On the Œsophagus. It is very exceptional for the œsophagus to be compressed, and therefore dysphagia is unusual.

From the surgical point of view an intrathoracic goitre presents difficulties which are not present in the treatment of a normally placed goitre. Engorgement of even the smallest superficial vessels may be responsible for excessive bleeding. Proximity of the goitre to the large veins of the thoracic inlet may be a source for serious bleeding, but this can be prevented if care is taken to keep within the fascial capsule of the gland, likewise if the enucleation of the goitre be conducted in this plane there is less risk of opening the pleura. Delivery of the goitre is facilitated by traction on the affected lobe or its connecting pedicle, but when it is very bulky it may be impossible to release it from the mediastinum unless it be diminished in size by excavation of its contents if that has not already occurred accidentally. Division of the sternum to increase the diameter of the thoracic inlet is only seldom necessary.

## DISEASES OF THE THYMUS GLAND

Knowledge of the function of the thymus gland and its biological effects at different epochs of life is still very scanty. More information about the suspected functions of the gland have accumulated from study of its pathological states than from physiological investigations.

The thymus is a ductless gland, entodermal in origin and derived as a tubular outgrowth from the third and possibly the fourth branchial segments of the embryo. The thymus is more conspicuous at birth than later; it is asymmetrically bilobed and lies immediately behind the manubrium sterni and overlies the pleura, great vessels and the pericardium. It is lobular in structure and its individual lobules consist of cortex and medulla; the former mainly lymphocytic in structure and the latter collections of translucent branched reticulum cells which in places assume a whorled formation and surround cells the seat of hyaline degeneration (Hassell's corpuscles).

In adolescence the thymus shrinks and is largely replaced by fat. The epithelial elements persist in reduced number and size but involution is not always final because in a number of diseases the gland may enlarge or be the seat of tumour formation.

In infancy the thymus may remain unduly large and has been held responsible for obstructive dyspnoea (thymic asthma). In such circumstances the thymus shares in a generalized overgrowth of lymphoid tissue throughout the body (status thymo-lymphaticus). Evidence

is lacking that enlargement of the thymus alone is responsible for asphyxia

The thymus gland may be enlarged, though not constantly, in many diseases notably Addison's disease, leukaemia of various kinds, and hyperthyroidism. Thymic enlargement in hyperthyroidism occurs in only a proportion of instances and its significance is not understood. The overgrowth is generalized and is unspecific in character. At one time it was suggested without foundation that the thyroid and thymus were linked functionally, and that the thymus gland regulated or modified the thyroid hormone.

Aberrant elements of thymic tissue have been found in the thyroid and parathyroid glands and in the areolar tissue of neck and in these situations have been responsible for cyst formation.

### The Thymus in Myasthenia Gravis

Since it was discovered early in the century that myasthenia gravis might be associated with a simple tumour of the thymus, continued efforts have been made to establish the relationship between the thymus and this obscure neuromuscular disorder. Considerable progress has been made.

During recent years it has been demonstrated that removal of a thymic tumour, an enlarged gland, and also the normally involuted gland may confer total or partial relief in a small proportion of cases of myasthenia especially in young subjects in which the disease is of short duration. A tumour (usually an encapsled adenoma) is present in about 10% of cases of myasthenia, in the absence of tumour formation the gland is either hyperplastic or normal for the age of the patient, and no particular cytological changes have been discovered.

The part played by the thymus in the myasthenic state has been the subject of much speculation, and new data has gradually accumulated. The underlying neuromuscular defect in myasthenia is not fully understood but it is suspected that the normal stimulus to contraction of muscle fibres by liberation of a minute quantity of acetylcholine at the nerve plate is disturbed. In myasthenia it is believed that there is a biochemical defect of transmission due to immobilization of acetylcholine by a relative excess of the enzyme—cholinesterase—its normal inhibitor. Experiment has shown that the serum of myasthenic patients interrupts nerve transmission and interferes with the production of acetylcholine by nerve cells whereas the serum of patients undergoing treatment by prostigmin has no such effect. Another interesting observation in this connexion in myasthenia is the rapid aggravation of symptoms which follows release of an arm tourniquet after the hand muscles have been in vigorous exercise.

The neuromuscular phenomena of myasthenia gravis have been compared with the changes present after administration of curare which is known to inhibit the chemical stimulus to muscle contraction. Prostigmin which exercises an opposite effect (and antagonizes cholinesterase) is well known for its beneficial effect in controlling the neuromuscular defect in myasthenia. Such evidence lends colour

belief that the thymus independently or with other glands may produce an agent which inhibits the local production of acetylcholine requisite for muscle contraction

### Cysts and Tumours of the Thymus

*Cysts of the thymus are rare. Most often cyst formation is of lymphangiomatous nature and may result in a tumour of great bulk of similar character to cystic hygroma of the neck to which it is probably allied.*

*Tumours.* Reference has already been made to the occasional association of a thymic tumour with myasthenia gravis. The tumour is usually an adenoma. It may occur independently of myasthenia. The tumour is of variable size and encapsuled and in structure resembles roughly the normal gland pattern or may be composed only of reticulum cells with scattered lymphocytic collections.

The most important tumours of the thymus are of a malignant character—*thymoma*. Their histological pattern is very varied and it is difficult to formulate a satisfactory classification of all types. There are examples which are indistinguishable from chronic lymphadenoma. Others like primary lymphosarcoma or reticulum cell sarcoma (with fibrils) and finally

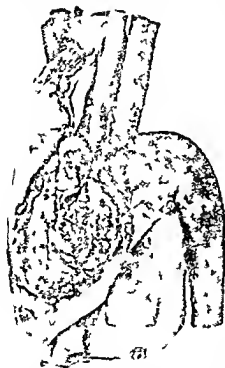


FIG. 15. An encapsuled carcinoma of the thymus gland from a man aged fifty nine years. The tumour had caused dysphagia. Death was due to purulent bronchitis. There were no metastases.

those in which there is a semblance of the normal gland pattern—epithelium and lymphocytes—are arranged in such a manner as to merit the title of adeno sarcoma or carcinoma sarcoma. In many instances leukæmic features with eosinophilia up to 20% is a prominent feature and may be of significance in diagnosis. Perhaps of even greater importance is their high degree of sensitivity to irradiation doubtless due to their high content of primitive lymphocytes.

At first the tumour conforms roughly to the bilobar shape of the thymus gland. It grows rapidly and assumes great bulk. It infiltrates the superior mediastinum and neighbouring organs and pressure effects on such important structures as the trachea and great vessels are not

long delayed—*mediastinal compression* Asphyxia is the usual mode of death. The tumour may extend to the neck, and penetrate the chest

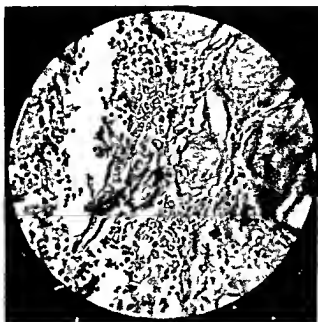


FIG. 158. Photomicrograph of thymic tumour depicted in Fig. 157 showing reticulum cells and lymphocytes



FIG. 159. Malignant thymoma, showing malignant lymphocytic tissue and a concentric laminated body

(Laboratory of Royal College of Physicians of Edinburgh)

wall. Extension to the cervical or the axillary glands is a common feature and may be the first evidence of the disease. Metastasis to distant organs is of rare occurrence.

Carcinoma of the thymus has been observed in association with cases of over-activity of the suprarenal gland.

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## CHAPTER XVII

### DISEASES OF THE PERICARDIUM, HEART, AND GREAT VESSELS

THE application of surgical measures to diseases of the heart and great vessels, and especially to congenital defects, has focussed attention upon the anatomical and pathological features of those conditions which lend themselves to operative correction. The advent of surgery to this province has called for a renewed study of congenital cardiac defects, for we still lack precise means of ascertaining the underlying structural abnormalities present in the living subject.

A résumé of the general pathological features of the more important "surgical" conditions follows.

#### DISEASES OF THE PERICARDIUM

**Suppurative Pericarditis (Pyopericardium)** is an occasional complication of blood infection by streptococci, pneumococci, and staphylococci. It is commonest as a sequel of such diseases as scarlet fever, osteomyelitis, and puerperal sepsis. When the infection is of staphylococcal origin multiple small abscesses in the heart muscle may coexist and add to the gravity of the disease.

The response of the pericardium to infection is the same as in the other serous membranes—exudation of a thin effusion with fibrin deposits and later pus. The post mortem appearances of the heart surface and pericardium are appropriately described as "shaggy," "bread and butter like," etc. The effects of the pericardial effusion, apart from the grave illness with which it is associated, are due to pressure and interference with full cardiac action—styled clinically as "cardiac tamponade." Embarrassment is seldom severe until the pericardial sac contains about half a litre of fluid. If the inflammatory process is gradual a much greater bulk is tolerated.

If suppurative pericarditis is survived widespread adhesion of the serous surfaces is inevitable. Such adhesion seldom leads to constrictive pericarditis, as no doubt the pericardium, once the acute process subsides, retains its elasticity.

**Tuberculous Pericarditis.** Tuberculous pericarditis may occur as a seemingly independent condition, but in most instances, especially in early life, there is tuberculous infection in the hilar glands, the pleura, or elsewhere. The evolution of the disease can be traced through a stage of simple effusion, caseation and loculation, to one of extreme fibrosis or calcification of the pericardium (see Fig. 156). In the severer cases caseous or calcareous nodules develop within the heart muscle.

If healing occurs the pericardium becomes thick, tough, and hyaline, and adheres to the heart surface either in patches, or over a broad

surface. This process is sometimes associated with severe mechanical effects on the chambers of the heart and is known as "chronic constricting pericarditis" —(Pick's disease).

**Chronic Constricting Pericarditis** As stated above this form of pericarditis is the outcome of thickening and stiffening of the pericardium. The underlying tuberculous nature of the condition is not doubted, but direct or even collateral evidence is not always obtainable.

The pericardium is not only thick and inelastic, but keeps the chambers of the heart fenced within a barrier of scar tissue, so that it is unable to receive or to expel the normal volume of blood.



FIG. 160 Extensive calcification of the pericardium in an adult with characteristic signs of constriction.

Congestive heart failure, evidenced by liver enlargement, leg oedema and a greatly elevated venous blood pressure ( $\times 4$ ) is a natural sequence.

Although the heart is entombed and smothered within dense adhesions it is little reduced in size, and the musculature though occasionally thin can recover if released from constriction. The coronary vessels are healthy. The orifices of the vena caval veins may be narrowed and even calcified but not to an extent which affects return of blood to the heart.

The chief and most important effect of constrictive pericarditis is reduction of the total output of the heart, the major factor in the mechanism is limitation of diastole (particularly of the ventricles), so that blood reaching the heart cannot be accommodated or propelled



The most significant effect of the reduced cardiac intake is registered on the venous side of the circulation. Thus veins in the neck may pulsate and the pressure readings are exceeded by three or more times normal. Liver enlargement with ascites is usual.

Measures designed to remove the restraining tissue have proved successful. It suffices to liberate the ventricles partially, so thin walled are the auricles that attempts at liberation are hazardous and not needed.

## CONGENITAL DEFECTS OF THE HEART AND GREAT VESSELS

Congenital anatomical defects of the chambers, valves and of the great vessels of the heart are present in about 3% of subjects. If the defect is survived, it may be the cause of varying degrees of disability and usually premature death. In some it passes unnoticed, and is compatible with surprising activity.

We are ignorant of most of the underlying causes of congenital defects of the heart and other organs. There is, however, evidence that infectious disease in the first few months of pregnancy interferes with foetal development and so produces congenital malformations. German measles is believed to be especially dangerous in this respect, though probably some other infections may have the same effect.

Maude Abbott collected, analysed, and catalogued a thousand examples of congenital cardiac defects and her work has proved of the greatest value. The anatomical variations may be simple or complex, and they often occur in combined and multiple form. From the practical standpoint the effects of structural abnormalities of either the heart or vessels (or both) will depend chiefly on whether (1) blood is diverted abnormally from the systemic circulation to the venous (pulmonic) side (as in patent ductus arteriosus and in some forms of patent inter-ventricular defect), or whether (2) venous blood is "shunted" to the systemic side of the circulation (as in congenital stenosis of the pulmonary artery and its associated defects). It will suffice to describe those conditions which have recently come within the range of surgical correction.

**Patent Ductus Arteriosus** Maude Abbott estimated that a patent ductus arteriosus was present alone in ninety-two instances in her 1,000 post mortem specimens. A patent ductus arteriosus is virtually an arteriovenous fistula between the aorta and the left pulmonary artery—persistence of the foetal state. At birth, it is believed that the process of closure is ensured rapidly by the contraction and fibrosis of a ring of musculature, aided no doubt by the reduced vascular tension following upon ventilation and expansion of the lungs. In exceptional instances closure may be delayed even to the age of ten years or later. Why sometimes there is persistent patency is a matter for speculation.

The duct is short, not more than a third of an inch, and its lumen though variable, is on average under half an inch in diameter. In rare instances aneurysmal dilatation of the duct occurs.

The net effect of a communication between the aorta and pulmonary artery is the same as in arteriovenous communication in large vessels more peripherally.

As about 30 to 50% of the ventricular output of the heart may be swung to the pulmonary circulation, the heart enlarges and the stem vessels and branches to the lungs dilate to accommodate the augmented blood flow. Effort increases the overflow into the pulmonary circuit and the reserve diastolic blood pressure is reduced to undetectable level. Cyanosis is absent usually, for already a plethora of blood reaches the lungs.

Hypertrophy of the left ventricle is an inevitable outcome of the long continued purposeless expenditure of effort, and it may culminate in heart failure at an early age. At first there may be little impairment of health save for retarded development, but the expectation of life is usually reduced on an average to twenty five to thirty years.

The most serious consequence of a persistent ductus is infection of the surface of the pulmonary artery—the equivalent of subacute bacterial endocarditis, and about 30% of subjects fall victim to this complication which formerly was invariably fatal. The continued impact of blood at high velocity against the pulmonary artery predisposes to weakening of the endothelium opposite the fistula and thrombosis results. Infection by streptococci especially *str. viridans*, is common, and a succession of infarcts in the lung may result in fatality.

Closure of the patent ductus has proved effective in arresting the infective process. Indeed, blood cultures previously yielding the infecting organism are rendered sterile almost immediately.

**Congenital Stenosis of the Pulmonary Artery.** The structural abnormalities in this form of defect are subject to considerable variation. The characteristic features, *inter alia*, are—(1) stenosis of the pulmonary\* artery and its branches and a bicuspid and narrowed condition of the pulmonary valve, (2) patency of the interventricular septum which may extend to within the aortic lumen (see Fig. 161), (3) enlargement and dilatation of the aorta, which may assume a rotated (dextra posed), overriding axis, i.e., crossing over the right bronchus before it assumes its normal position distally. Effective blood flow to the lungs is impeded, and the right ventricle hypertrophies enormously, the pulmonary cone is inconspicuous and the heart has a shape likened to a Dutch clog. Other abnormalities such as a coexistent patent ductus, aberrant or unusually thin pulmonary arteries, or even absence of a main artery are common. The combination of deformities, subject to variations, is known as the

Tetralogy of Fallot, and its clinical effects were long ago described as the "*maladie bleue*."

The above combination of defects is responsible for reduced blood flow to the lungs. Blood seeking oxygenation is re-carried to the systemic circulation through the septal defects. It is not surprising, therefore, that the two most conspicuous features are severe dyspnoea on the slightest effort and cyanosis. The expectation of life beyond the age of ten years is very low. Collateral features of anoxemia are polycythemia to a level as great as 10 000 000 red cells per c mm, and a hæmoglobin carrying level of as much as 180%. In this, as in other congenital cardiac defects, pressure readings and oxygen saturation

\* Congenital stenosis of the pulmonary artery as an independent defect is very rare, present only in about 9 per thousand abnormalities.

tests of blood from within the chambers of the heart (secured by a catheter passed via an arm vein) have been helpful in estimating the proportionate amount and quality of blood destined for the pulmonary circulation

It is to Blalock (Baltimore) and his associates and to Potts (Chicago) that we owe the ingenious devices whereby the pulmonary stenosis may be by passed to provide a channel whereby blood may reach the lungs for effective oxygenation

## COARCTATION OF THE AORTA

Congenital stenosis of the aorta immediately distal to the origin of the left subclavian artery is a rare but important cause of arterial



FIG 161 Congenital pulmonary stenosis with associated features of Fallot's tetralogy. The large right ventricle has been opened. The lower rod is within a patent interventricular septum which overlies the aorta. The upper rod is in a small aberrant artery which joins the left pulmonary artery distal to an area of atresia, an unusual malformation.

hypertension manifest in the upper part of the body. Maude Abbott found such a constriction present independently in 112 of a thousand examples of cardiovascular defects and that it had a proportionately higher incidence in males than females (3:1). In many instances (about 90%) coarctation is associated with a bicuspid formation of the aortic valve, a condition which predisposes to infective endocarditis.

In coarctation the stricture is situated at or about the level at which the ligamentum arteriosus joins the aorta. The narrowed section, tough and hyaline in texture, is about 4 to 5 mm. in length and in width less than a centimetre. The aortic lumen may be reduced to 2 or 3 mm. or there may be complete obliteration. Not only is the aorta constricted

but is indrawn by fibrous tissue which connects it to the pulmonary artery and the adjacent mediastinal tissues

The calibre of the aorta distal to the stricture is subject to variation it may be normal, or it may be greater than normal, in a few (10%) it is reduced in diameter and its coats may be poorly developed The subclavian artery proximally is dilated The intercostal arteries, the major links in the collateral blood supply to the lower part of the body are large and tortuous, and the direction of blood current within them is reversed

Coarctation of the aorta is responsible for elevation of blood pressure in the main arteries of the head and neck and upper extremities, and diminution in those distal to the stenosis The compensatory collateral channels are according to anatomical pathways, so that dilated and pulsatile vessels are obvious in the axilla, the chest wall, and the interscapular region In some instances the dilated and tortuous intercostal arteries cause notching or exaggeration of the normal vascular groove in the under margin of the ribs

In coarctation the long sustained high blood pressure—it may (even in childhood) be as much as 180 mm of Hg in the arm compared with 90 mm in the leg—predisposes to hypertrophy of the heart dilatation and atheroma of the aorta and finally failure from aortic valve incompetence Other causes of early death are cerebral hemorrhage, rupture of the heart and infective endocarditis It is not surprising that the average length of life in coarctation is low, probably not more than thirty five years

If the local anatomical conditions allow, resection of the stricture succeeds though in some instances the stenosis involves so great a length of the aorta that restoration of continuity of the vessel would be impossible

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## CHAPTER XVIII

### DISEASES OF THE BREAST

#### STRUCTURE OF THE BREAST

THE epithelium of the breast, the lining membrane of its ducts and acini, is derived from the epidermis on the ventral aspect of the foetus, and the breast may be regarded as a collection of greatly modified sweat glands. The first indication of the developing breast is to be found in the second month of intra-uterine life. At this period the ducts, twelve to twenty in number, appear on the deep aspect of the epidermis and extend as solid cords into the superficial fascia, from which they derive a supporting framework. The ducts become canalized, branch repeatedly and form abundant lobules, which extend into the surrounding fibrous tissue. From their blind extremities the acini develop. The acini are scanty and ill developed until puberty, after which they show a remarkable faculty for periodic proliferation and retrogression.

The fully developed breast consists of a number of lobules, each somewhat pyramidal in shape and supported by a framework of tough fibrous tissue. On the superficial aspect, this framework is attached to the deep surface of the skin by the suspensory ligaments (ligaments of Cooper).

The ducts, deep to their orifices, expand just below the nipple to form ampullæ, which serve as reservoirs for milk. At the nipple the ducts are lined by squamous epithelium continuous with the skin, and as they are narrow they are liable to be occluded, either by periductal fibrosis or by epithelial debris in the lumen. Below the nipple the ducts are lined by a double layer of columnar or cubical epithelium supported by connective tissue containing both elastic tissue and plain muscle fibres. As the terminal ducts are approached the elastic tissue and muscle fibres gradually diminish in number, and the acini which in the virgin breast are scanty and small are lined merely with epithelial cells and a basement membrane. Ducts and acini lie embedded in an abundance of areolar tissue, which is in turn bounded by the tougher supporting framework of the gland. The delicate tissue immediately surrounding the acini fulfils an important rôle, for during pregnancy and lactation it provides a ready 'accommodation space' for the immense proliferation of secretory cells then required.

**Physiological Changes in the Breast.** In infancy and childhood the breast remains undeveloped, and consists principally of the larger ducts embedded in fibrous tissue. Acini are scanty, and those present are of small size. In the male this state persists throughout life, but in the female the gland undergoes remarkable changes in preparation for its functional activity during the reproductive period.

The first of these changes usually begins at puberty. At this time the breasts increase in size slightly, the ducts branch and rebranch, and from their extremities alveoli of secretory cells bud out. Occasionally this physiological hyperplasia may be exaggerated, marked by temporary enlargement and tenderness of the breast, or even by the secretion of milky fluid—"puberal mastitis." A similar transient phase of activity may occur in the new-born—"mastitis neonatorum."

Puberty past, the breast enters upon its virginal phase, which continues until interrupted by pregnancy and lactation or until the advent of the menopause. The virgin breast is generally in the state described above, and its acini are scanty and small. Yet, the gland is not entirely inactive, but is subject to recurring phases of proliferation and retrogression at the menstrual periods. Coincident with ovulation and the formation of the corpus luteum the epithelium lining the terminal ducts proliferates, and the acini increase both in size and in number. Failing impregnation, and when the stimulus associated with the menstrual period ceases, the newly formed acini shrink and disappear, and the breast returns to its normal intermenstrual condition.

In pregnancy and lactation the breast attains its zenith of physiological activity. Towards the latter part of pregnancy the cells lining the acini proliferate, and innumerable new acini bud out, pushing aside the lax peri-acinar areolar tissue and occupying every available space, even filling and enlarging the nipple. The secreting cells become columnar in shape, and almost fill the acini, and the whole picture is thus one of immense physiological activity.

*Involution.* At the end of lactation, and again more completely at the menopause, the breast undergoes a process of involution, whereby it becomes reduced in size, often to a thin fibrous remnant which is barely palpable even in thin subjects. The microscopic changes are varied, for involution is characterized both by atrophy and by a certain amount of proliferation. Many of the epithelial cells of the ducts and acini disappear entirely, but a few remain and may proliferate to form minute cysts or solid epithelial buds. The stroma of the breast becomes thickened by fibrosis, so that the delicate peri-acinar tissue becomes lost in bands of tough scar. The elastic lamina, previously a thin layer principally limited to the walls of the ducts, may become increased in amount and may spread around the acini. Often there is a lymphocytic infiltration of the stroma.

The involution process is one of peculiar interest in relation to many diseases of the breast. Involution changes are so common in a breast after the menopause that they are often regarded as normal, but it should be recognized that they are not merely the changes of senescence and decay. The involuting breast is the site of proliferative activity as well as of atrophy, and in some cases the proliferation may approach that seen in "chronic mastitis."

### MASSIVE HYPERTROPHY OF THE BREAST

Diffuse enlargement of one or both breasts may result from tumours, cysts, or other circumscribed lesions, or it may occur as a manifestation

of general obesity, but the term "massive hypertrophy" refers to an entirely distinct condition in which there is a diffuse overgrowth of one or more elements of the mammary gland proper

Massive hypertrophy is a very rare disease, and there are fewer than 100 authentic cases on record. Almost invariably the disease affects both breasts, though not always equally. In the great majority of cases it commences at puberty (puberal hypertrophy), but occasionally it has appeared during pregnancy or lactation.

The breasts gradually increase in size, and in the course of a year or two may attain the weight of a kilogram or even more, and hang to the level of the thighs. There is no commensurate increase in functional activity, and after childbirth there may be no secretion of milk. The skin of the breast becomes dusky and congested and sometimes thickened, and the superficial veins may be distended. The areola is enlarged and deeply pigmented. The breast tissue is soft and sometimes nodular.

The enlargement is diffuse and affects principally the fibrous stroma of the gland, although there is also some overgrowth of the epithelial elements. Naked eye examination reveals no characteristic change, there is nothing but "prodigious bigness." On microscopic examination there is sometimes a resemblance to the intracanalicular type of fibro adenoma to which it may be related.

Massive hypertrophy is usually accompanied by amenorrhœa, and other developmental anomalies of the reproductive organs. Such features, together with the period of onset and its bilateral nature, suggest that the cause is some perversion of internal secretions probably of ovarian or hypophyseal origin.

The rapidity of the enlargement sometimes leads to a suspicion of malignancy, but actually malignant change is rare. A more important complication is infection, which may be of severe type.

### ACUTE MASTITIS AND MAMMARY ABSCESS

This is an acute bacterial inflammation of the breast. Apart from rare cases in which the infection complicates tumours or cysts or other existing lesions, it occurs almost always during or shortly after lactation. The organism is usually *staphylococcus aureus*, less commonly a streptococcus, and the infection reaches the breast either from a fissure in the region of the nipple or along the milk ducts. In exceptional cases, unrelated to lactation, the disease may follow hæmatogenous infection, e.g., in typhoid fever.

The disease takes an acute course, with swelling, engorgement of the breast, and with much pain and severe constitutional upset. Sometimes resolution occurs after a few days, with complete restitution of the gland, but often suppuration ensues and a mammary abscess results.

Suppuration is favoured by the congestion of the breast and its milk content. One of the first effects of the inflammation is to obstruct the orifices of the milk ducts, and the retained secretion, which rapidly clots, forms a fertile medium for bacterial growth. During lactation

the breast is at the height of its functional activity, and its lobules contain large numbers of highly specialized, easily damaged, secreting cells. The lobules are separated and closely walled in by tough fibrous septa. Any inflammatory swelling, therefore, is at first confined under tension, and much necrosis of the soft parenchymatous elements results. When eventually the pus bursts its confines it tracks widely through adjacent lobules forming an irregular multilocular cavity, traversed by fibrous bands.

It is customary to describe three varieties of mammary abscess, according to their position in, behind, or in front of the gland. In an intra mammary abscess the infection spreads from lobule to lobule, perhaps involving the greater part of the breast. Suppuration is slow to develop and is associated with much damage to the secreting tissue. If the abscess arises superficially in the breast, or in an outlying glandular lobe in the nipple or under the skin, it rapidly spreads to the subcutaneous tissue—one form of *pre mammary abscess*—and in this situation it points rapidly with little damage and few constitutional symptoms. Pre mammary abscesses may arise also from infection of a sebaceous gland or from superficial cellulitis and in such a case the breast is not affected.

A deep-seated intra mammary abscess may spread to the connective tissues behind the breast—*retro mammary abscess*. Such an abscess may have the shape of a collar stud with a small cavity in the deeper part of the breast communicating with a larger one in the retro-mammary connective tissue plane. Rarely a retro-mammary abscess arises from other causes e.g. secondary to an infected hæmatoma or to osteomyelitis of a rib.

### CHRONIC MASTITIS (Cystic Mastitis)

This is a disease of confused nomenclature, complicated morphology and baffling pathogenesis, and it has been described as the "root and centre of all difficulties in breast pathology." It is now clearly recognized that the disease has a far greater significance than that of a mere inflammation but its true nature is still a subject of controversy. This is reflected also in the diversity of nomenclature adopted by different writers for cystic mastitis, diffuse fibro-adenoma, involution disease, and a host of other names have been applied. The term 'chronic mastitis' is unsatisfactory, for it indicates an inflammatory lesion but it has received general adoption and for the present it may therefore be retained.

The features of chronic mastitis are many and varied, but three stand pre-eminent, namely (1) capricious fibrosis of the peri acinar and periductal tissues, (2) cystic dilatation of acini and ducts, and (3) widespread proliferative changes in the epithelial lining cells.

On section, the corpus mammae is tough and fibrous, of grey or greyish yellow colour and of the consistency of indiarubber. It differs from a scirrhus carcinoma in lacking the stony hardness of that condition and in containing none of the characteristic small yellow spots of epithelial debris. Cysts are usually, though not invariably, present. Most often they are small, only a few millimetres in diameter, and



scattered through the whole substance of the breast, but occasionally there is a solitary cyst, or two or three are present, and they may attain considerable size. Rarely the whole breast is occupied by large cystic spaces (cystic disease of the breast, Schimmelbusch's disease, Réclus' disease). The main ducts of the breast are often visibly dilated, and filled with creamy fluid or soft yellow *débris*. The content of the cysts may be of similar nature, but it is usually thin and watery, either clear or slightly turbid, rarely blood stained. When the cysts are large they project beyond the confines of the actual gland, and form tense rounded swellings. Such cysts, distended with clear fluid, have a blue colour when exposed by incision of the tissues overlying them, and have been called blue domed cysts (Bloodgood). Sometimes the cysts contain papillomatous growths (Brodie's tumours), and although these are usually small and barely recognizable without the aid of a lens, they may occasionally attain considerable size. Thus it is possible to trace

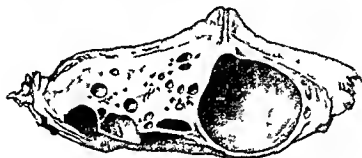


FIG 102 Chronic mastitis. The breast is fibrous and contains numerous cysts

(By courtesy of Mr J W Struthers)

all intermediate forms between simple chronic mastitis and true benign tumours (papillomata and adenomata)

**Microscopic Appearance** The microscopic appearance is very varied, both in different breasts and in different parts of the same breast. In one region fibrosis predominates in others cyst formation, and in yet others epithelial proliferation.

The fibrosis affects principally the delicate periacinar and periductal connective tissues. The new fibrous tissue is often infiltrated with lymphocytes and plasma cells, and the elastic lamina, previously a tenuous layer related only to the ducts may extend to enclose the acini. The cysts vary greatly in size and shape. They contain fluid and epithelial *débris* and often large masses of cells derived from the duct wall. Some of the cysts are lined by cells similar to those of normal mammary ducts others by somewhat larger pale staining eosinophil cells. These 'pale cells' closely resemble the epithelial cells of sweat glands and have been regarded as sweat gland rests of developmental origin. More probably they are derived from the ordinary cells of the breast itself a modified sweat gland. According to Cheate the cysts arise principally from dilatation of the ducts and in serial sections it is sometimes possible to trace the whole length of a duct with its branches and related acini as a long, tortuous, dilated channel.



FIG. 163. Chronic mastitis.  $\times 100$ . There are several dilated ducts. Below on the right a duct is distended as though from obstruction and the epithelial lining is flattened. Above on the right a dilated duct contains a laciform papillomatous mass of proliferated epithelial cells. The connective tissue between the ducts is fibrous and is infiltrated by lymphocytes.

(Royal College of Physicians of Edinburgh)

The cause of the cyst formation is not definitely settled. By some it is attributed to fibrosis and consequent distortion or obstruction of the ducts; by others to excessive proliferation of the lining membrane. It is likely both these factors operate for in some places the lining membrane is atrophied and flattened as though from distention while in other parts it shows evidence of active growth and proliferation.

**Epithelial Proliferation in Chronic Mastitis**  
The epithelial proliferation or hyperplasia is now regarded as the most conspicuous feature

of the disease. The proliferation takes many forms, all of which may be recognizable in a single breast, and there may be a continuous gradation in different parts of the breast or in a single duct, from simple overgrowth to hyperplasia indistinguishable from malignancy.

E. H. Dawson recognizes two main types of proliferation: adenosis and epitheliosis. *Adenosis* denotes proliferation which though excessive still conforms to the physiological pattern and consists in an increase of glandular tissue similar to that in pregnancy. Such adenosis may affect the whole breast or occur in localized areas. When present in excess it may lead either to a diffuse adenomatosis or to one or more localized tumours (fibro-adenoma).

*Epitheliosis* denotes an increase of epithelium which does not form glandular tissue of physiological pattern but which fills up and distends existing glandular structures (ducts or acini). Such epitheliosis may consist in a simple overgrowth of the epithelial lining cells or in papillomatous proliferations.

In the papillomatous type of proliferation the lining cells multiply and are projected into the lumen upon delicate cores of connective tissue. Such proliferations are common in chronic mastitis and occur either in dilated ducts or in cysts. Generally, they are found only on microscopic examination but one or more may attain considerable size and present all the characters of a simple tumour (duct papilloma or intra-cystic papilloma).

The massive type of epithelial proliferation is the least common. The ducts are filled by solid masses of hyperchromatic cells which show every sign of rapid growth. The cells individually appear malignant.

and can be distinguished from invasive carcinoma only in that they are confined to the lumen and do not invade the surrounding tissues. Such a condition approximates closely to the "intraduct carcinoma" described by Muir.

**Types of Chronic Mastitis** Two main forms of chronic mastitis may be recognized clinically, the *localized* and the *diffuse*. The *localized form* affects principally one segment of the breast, although microscopic examination generally shows that the changes are not entirely circumscribed, but are present over a wide area and in both breasts. The affected part forms a nodular, irregular lump in the breast, and some times is so hard as to simulate cancer. It may usually be distinguished, however, by the fact that although easily palpable and clearly outlined when the breast is held between fingers and thumb, it loses both its definition and its sense of induration when pressed against the chest wall. In other respects the distinction is not always easy. Chronic mastitis rarely causes retraction of the nipple or dimpling of the skin, but since these two signs may be absent in the early stage of cancer—the ideal stage for treatment—their diagnostic value is limited. Moreover, in mastitis slight enlargement of the axillary glands is not uncommon and it may prove misleading.

The *diffuse form* affects the greater part of one or both breasts, and for this reason is less likely to be mistaken for malignant disease. The characteristic feature is a diffuse, fine granularity, most easily defined when the breast is palpated between the fingers and thumb.

Cysts may occur in either type, and if large are readily palpable as smooth, tense, mobile swellings. In some cases, one or both breasts are completely cystic (Schimmelbusch or Réclus' disease).

Chronic mastitis may develop about the period of the menopause but often it occurs much earlier. It is most common in the unmarried and childless, but may arise in parous women. In the majority of cases it is symptomless and passes unnoticed or only attracts attention when a lump is felt in the breast. Occasionally, however, there are shooting pains either in the breast itself or referred to the arm.

**Nature of Chronic Mastitis** The nature of chronic mastitis has been greatly clarified in recent years. All the available evidence indicates that the disease is not due to bacterial infection nor to toxæmia but to the perverted action of certain hormones which normally exercise an influence upon the activities of the breast.

The breast is continuously influenced by ovarian hormones which are themselves subject to the control of the hormones of the anterior part of the pituitary gland. To variations in the activity of these secretions are due those proliferative changes which occur at puberty, at the menstrual periods, during pregnancy and lactation, and at the menopause. It can readily be understood, therefore, how an abnormality of this controlling mechanism may lead to the changes characteristic of chronic mastitis, changes which differ from the physiological process of involution only in their greater extent and in the predominance of epithelial proliferation rather than atrophy.

So far as our present knowledge goes, both the ovarian hormones, œstrin and lutein, exercise an effect on the breast, and it is possible

that pituitary hormones may act both directly on the breast and also indirectly by controlling the secretions of the ovary. In animals it has been found possible to induce chronic cystic mastitis by repeated injections of impure folliculin or œstrin (Goormaghtigh), and it seems likely that some abnormality, quantitative or qualitative, in these hormones is responsible for chronic mastitis in man.

**The Relation of Chronic Mastitis to Tumours of the Breast** (1) *Simple tumours*. Chronic mastitis is an almost invariable accompaniment of simple tumours of the breast. Generally, it can be recognized only on microscopic examination but in some cases its presence is quite obvious. Some authorities indeed, recognizing the close relationship of chronic mastitis to simple tumours, regard them not as distinct conditions but as manifestations, differing only in degree, of a single disorder, a mammary dysplasia. Thus a fibro-adenoma may be regarded as an extreme, localized form of the "adenosis" found diffusely in chronic mastitis whilst a papilloma may be regarded as an extreme, localized form of 'epitheliosis'.

(2) *Carcinoma*. The relation of chronic mastitis to carcinoma is of immense interest in its bearing upon the question of the cause of cancer and it is also of great practical importance from the therapeutic standpoint for upon it depends the choice so vital to the welfare of the patient between conservative measures and radical extirpation. In spite however of extensive clinical and pathological investigations the question still remains highly controversial and eminent authorities hold opposite views viz (1) that chronic mastitis is a frequent precursor of cancer and (2) that the breast affected with chronic mastitis is little if any more liable to cancer than the normal breast.

The close relation of mastitis to cancer has been upheld principally by those who approach the subject from the histological standpoint, and there is no doubt that on microscopic examination the epithelial proliferation of mastitis may approximate so closely to malignancy as to deceive the most experienced pathologist. Moreover, a breast affected by carcinoma almost invariably shows evidence of chronic mastitis. These observations afford very strong support for the view that at least some forms of chronic mastitis are precancerous. Further support has recently been forthcoming from experimental work upon the hormonal origin of chronic mastitis, for it has been claimed that in mice the repeated injection of folliculin (œstrin), which has been shown by other writers to give rise to chronic mastitis, may in some cases lead to the development of carcinoma (Lacassagne).

From the practical standpoint, however, it must be recognized that malignant change is not a regular, or even a frequent complication of chronic mastitis. The general view is that carcinoma is most likely to occur in the localized type of chronic mastitis, especially if cystic, and that it is a very rare complication of the diffusely nodular type.

### CYSTS IN THE BREAST

The great majority of cysts in the breast are those related to chronic mastitis, and have already been described.

A rather uncommon type of solitary cyst is the *galactocoele*, or milk cyst. It develops during or shortly after lactation, probably from obstruction to one of the principal ducts. At first the content is thin and milky, and the cyst is tense and thin walled, but finally the milk gradually becomes inspissated, and the wall loses its epithelial lining and becomes thick and fibrous, so that it may eventually resemble and be mistaken for, a dermoid cyst. It forms a painless, rounded swelling situated close under the nipple. At first it is tense and elastic and is mobile within the breast. Sometimes a little milky fluid may be expressed from the nipple. Later it acquires a more solid consistence and becomes fixed to the surrounding breast by fibrous adhesions. The history of onset during lactation usually suggests its origin.

Cysts may arise in the breast in relation to tumours, and they will be described in the appropriate place. Blood cysts occasionally arise from the encapsulation of old hæmatomata. The so called retention and lymphatic cysts are probably really cysts in connexion with chronic mastitis.

### TUBERCULOSIS OF THE BREAST

This affection occurs principally in middle aged women. It is a rare condition though like other forms of tuberculosis it is not uncommon in Scotland.

The breast is usually involved by direct spread of the disease from some neighbouring structure, *e.g.*, from a rib, from a lymph gland in the axilla or from tuberculous pleurisy. Rarely, it is involved in the absence of a neighbouring focus, and the infection must be presumed to have reached the breast by the blood stream.

In the common form, secondary to tuberculosis of a costo chondral junction, there is a deep seated, symptomless swelling—a cold abscess—which may track forwards and downwards, involving the mammary tissue. Eventually it comes to the surface, generally at the infra mammary fold, and gives rise to a sinus.

Less often, in the early stages a hard nodular mass may be felt in the breast, and may be mistaken for a focus of chronic mastitis or even carcinoma. It consists of an aggregation of tubercles, partly caseous and matted together by fibrous tissue. Such a mass generally softens, and in the course of time gives rise to a cold abscess, or it may stimulate much fibrous tissue and lead to extensive sclerosis of the breast.

### SIMPLE TUMOURS OF THE BREAST

These are fibro-epithelial tumours composed of various proportions of glandular and connective tissues. In the past it has been customary to recognize a large number of different types, but it is now admitted that many of these depend merely upon variations of degree rather than of kind, and that actually all are closely related. The most simple and generally useful classification recognizes three principal tumours, two forms of fibro adenoma and one form of papilloma. Typically, each of these is distinguished by striking characteristics, but intermediate forms may occur in which the designation is difficult.

In regard to the aetiology of these tumours, a great advance has been achieved in recent years. By the employment of whole section, "key block," and other methods it has become possible to study the

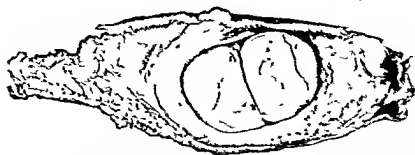


FIG 164 Pericanalicular fibro-adenoma of the breast, removed from a woman aged twenty-eight years. The tumour had grown slowly during several years. It is non malignant, and is surrounded by a well defined capsule of condensed fibrous tissue.

(Department of Surgery, University of Edinburgh.)

breast as a whole. Such studies show clearly that a simple tumour is rarely the only pathological lesion, but is often accompanied by changes of the nature of chronic mastitis in the rest of the breast; and there is

much evidence to suggest that the two lesions are connected, and that the tumour may be regarded as a very localized and extreme form of the same proliferative changes as exist in chronic mastitis.

Simple tumours other than fibro-adenoma and papilloma are rare. Fibroma, adenoma, lipoma, myxoma, and angioma have been described.

#### Fibro-adenoma

Two principal types of fibro-adenoma are recognized: (a) pericanalicular and (b) intracanalicular.

FIG 165 Pericanalicular fibro-adenoma of the breast. Acini lined by a single layer of columnar or cubical cells lie embedded in a fibrous stroma.

(Laboratory of Royal College of Physicians of Edinburgh.)

(a) **Pericanalicular Fibro-adenoma.** A pericanalicular fibro adenoma occurs typically in young women from twenty to thirty years of age, though occasionally later in life. It is usually small, firm, and of slow growth (hard fibroma), but may be softer, even to the softness

of a lipoma. It is rounded or ovoid, and almost invariably encapsuled, and is mobile within the substance of the breast. When the capsule is opened and incised the tumour may be enucleated like a pea from its pod, and like the pea it has a pedicle of attachment where its vessels enter.

The pericanalicular fibro adenoma is believed to arise as a result of an extreme but localized proliferation comparable to the "adenosis" of chronic mastitis (p. 374). It is as though a ductule or a number of related ductules bud out into innumerable new acini, which fill the "accommodation space" and hollow out a cavity for themselves within a capsule formed by the surrounding fibrous tissues.

The microscopic structure is extremely simple, for the tumour consists of a variable amount of fibrous tissue in which are rounded or oval acini lined by cubical epithelium. Depending upon the amount

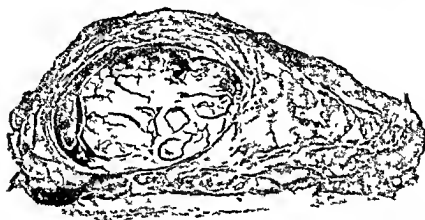


FIG. 16c. Intracanalicular fibro adenoma of the breast. The tumour forms a cauliflower like growth and fills and distends the cyst in which it lies.

(Department of Surgery, University of Edinburgh)

and nature of the connective tissue, the tumour is soft or hard. Occasionally, when the stroma is scanty, the appearance is that of an adenoma, and when the stroma preponderates the tumour may have the character of a fibroma.

(b) **Intracanalicular Fibro-adenoma.** An intracanalicular fibro adenoma differs both in appearance and progress. It occurs commonly at a later age period (between thirty and fifty years) and grows somewhat rapidly. The consistence is soft and eventually the tumour may attain great size and is liable to be mistaken for sarcoma. On section the tumour appears partly cystic and partly solid and in places the solid portions project into the cysts in the form of bulky cauliflower like processes of complicated structure (*cystadenoma* or *intracystic papillary adenoma*).

The tumour probably arises from overgrowth of the delicate connective tissue immediately outside the ductal epithelium. In its growth this tissue projects into ducts and dilated spaces in a complicated mass of blunt, rounded processes each covered with epithelium. With

increase in size these processes adhere and form secondary attachments to the duct or cyst walls. This complex three-dimensional

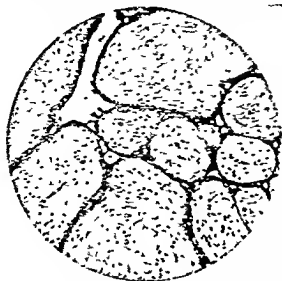


FIG. 167 Intracanalicular fibro-adenoma of the breast.  $\times 100$  There is an overgrowth of lax, oedematous, connective tissue, and this, projecting into the dilated mammary ducts in complex fashion, has earned with it a covering of cuboidal epithelium.

(Laboratory of Royal College of Physicians of Edinburgh.)

With increase in size it becomes irregularly lobulated, and its shape is modified by cyst formation. Later it may adhere to the deep surface of the skin, and by pressure may finally fungate. This appearance, now rarely encountered, may suggest malignancy, hence the old name "cysto-sarcoma fungoides."

### Duct Papilloma (Intracystic Papilloma)

This is an epithelial tumour arising from the lining cells of a large duct, and projecting into the lumen of the duct, which coincidentally becomes dilated or even cystic. It is slow-growing, and occurs usually about the period of the menopause, though occasionally in younger women.

It is recognizable as a rounded mass of any size up to that of a hen's egg, generally situated close under the nipple, which may be unduly prominent or retracted. Associated with the tumour there is a discharge of clear or sometimes blood-stained fluid from the nipple.

On cut section the tumour is seen as a papillary growth projecting from the wall of a dilated duct. It may be small in comparison with the dilated space or it may occupy the entire cavity, to which it is often adherent at numerous points.

Microscopically, it consists of a complex dendritic core of delicate connective tissue surmounted by hyperplastic columnar epithelium

growth is not easily recognizable in sections, and microscopically the tumour consists merely of large tracts of connective tissue containing slit-like, semilunar or irregularly branching spaces lined by cubical epithelium. The connective tissue of the tumour is extremely delicate, of almost myxomatous appearance, and it may be so cellular as to resemble sarcoma. Sarcomatous change occasionally takes place (*adenosarcoma*).

The tumour at first is mobile and on incision it may be shelled from a definite capsule.



either in a single layer or, more frequently, several cells in depth. Usually only one palpable tumour is present in the breast. Rarely there may be two or three of approximately equal size. As Cheate has emphasized, however, careful examination frequently reveals early



FIG 108 Duct papilloma of the breast—5/6 natural size. The tumour has projected into and distended one of the main ducts of the breast. The duct is cut across in two places in the nipple and deeper in the breast and portions of the extensive papilloma are seen in each situation. The underlying breast shows very well the 'adenosis' of chronic mastitis.

(Laboratory of Royal College of Physicians of Edinburgh.)

changes of a similar nature widely distributed throughout the breast.

A duct papilloma is apt to undergo malignant change and discharge of blood from the nipple is suggestive evidence of its occurrence. Some authorities believe that duct papilloma is itself in the early stages of malignancy. It is certainly to be regarded as precancerous.

## MALIGNANT TUMOURS

### CARCINOMA

Four of every five tumours in the breast are malignant, and of these the vast majority are carcinomata. Sarcoma and other rare growths account for only 3%. Carcinoma of the breast is, moreover, one of the commonest of all malignant tumours sharing this distinction with carcinoma of the uterus but fortunately, owing to its accessible position and comparatively slow growth, its recognition is often possible in the early stages, at a time when it is amenable to treatment.

The disease is almost limited to women, and less than 1% of cases occurs in men. It appears most commonly between the ages of forty and sixty, but it has been known to arise at the early age of seventeen, and it is not uncommon in the aged. Nulliparae are somewhat more liable to be affected than multiparae, owing perhaps to the frequency of chronic mastitis in the former.

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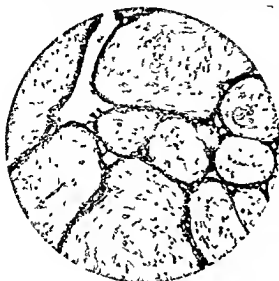


FIG 16" Intracanalicular fibro-adenoma of the breast  $\times 100$ . There is an overgrowth of lax, oedematous connective tissue, and this projecting into the dilated mammary ducts in complex fashion has carried with it a covering of cuboidal epithelium.

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FIG 168 Duct papilloma of the breast— $\frac{2}{3}$  natural size. The tumour has projected into and distended one of the main ducts of the breast. The duct is cut across in two places in the nipple and deeper in the breast and portions of the extensive papilloma are seen in each situation. The underlying breast shows very well the adenosis of chronic mastitis.

(Laboratory of Royal College of Physicians of Edinburgh)

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**Types of Mammary Carcinoma.** In the past an extremely complicated classification of carcinoma of the breast has been adopted but nowadays the whole trend of informed opinion is in favour of simplification.

The extensive researches of Cheate and Cutler, Dawson and others have demonstrated that the tumours so variously described are not distinct neoplasms but variations from a common type, and that the differences in histological structure are variations in degree rather than in kind.

The subject can best be studied by considering the early phases in the development of a tumour from its original cell or cells. It may be

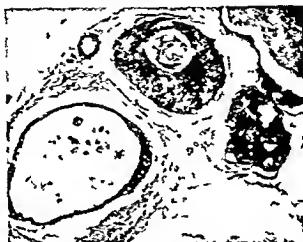


FIG. 169. Intraduct cancer of the breast.  $\times 10$ . Two of the ducts are occupied by solid masses of epithelial cells which have all the characters of malignant cells except that they do not invade the surrounding tissues. The other two ducts are dilated and contain cells of colostrum type. Their lining cells show early proliferative changes.

(Laboratory of Royal College of Physicians of Edinburgh.)

assumed that practically all carcinomata in the breast arise from the epithelium of the duct system or of cysts derived from the duct system. They may all, therefore, be regarded as forms of *duct carcinoma* although this term is used by some authorities in a more limited sense, to signify tumours characterized microscopically by duct or tubule-formations.

The original epithelial cells, when stimulated to malignancy, may at first proliferate entirely into the lumen of the duct or cyst, without invading the surrounding tissues. To this condition of intraductal malignant epithelial proliferation Muir has applied the term *intraduct carcinoma* (see Fig. 169). Such proliferation may occur diffusely, affecting a large number of cells simultaneously in more than one part of the breast. In some cases it gives rise to a localized tumour—an *adenocarcinoma* characterized microscopically by the presence of tubules lined by several layers of hyperplastic epithelial cells (see p. 384).

The next stage in the progress of the malignant cells is seen when

they penetrate the basement membrane of the duct wall and invade the surrounding connective tissues. With the assumption of invasive character, both the microscopic picture and the degree of malignancy show an immediate change. The cells, originally cylindrical, now by mutual pressure assume a spheroidal shape, and they no longer give rise to tubular or acinar formation but grow into the tissue and lymph spaces in the form of solid processes. In this way originate the various forms of *spheroidal-cell carcinoma* of the breast a term which embraces the common scirrhus tumour and rare forms such as the encephaloid carcinoma and the acute carcinoma of lactation.

The malignancy of the various forms of invasive carcinoma of the breast depends upon the functional activity of the affected gland. In an atrophic breast of diminished vascularity and scanty lymph drainage malignant cells progress slowly and become enveloped in a stroma of dense fibrous tissue (*atrophic scirrhus carcinoma*), whereas in a well-developed breast of full vascularity and free lymph drainage progress is rapid the malignant cells grow in large solid masses and the stroma is scanty (*encephaloid or medullary carcinoma*). The most malignant mammary carcinoma is that which affects the gland in pregnancy or lactation when its functional activities are at their zenith and its high vascularity and copious lymph drainage favour intense proliferation and early dissemination.

### Scirrhus Carcinoma

A hard or scirrhus carcinoma is the commonest form of mammary growth occurring characteristically in women between the ages of thirty five and sixty five. The growth is situated most often in the

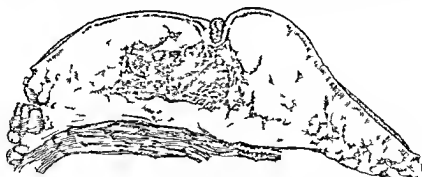


FIG 170 Scirrhus carcinoma of the breast. The tumour possesses no capsule and has infiltrated the tissues of the breast. The nipple is deeply retracted.

(Department of Surgery University of Edinburgh)

upper outer quadrant of the breast, least often the lower inner quadrant is affected, while the other two quadrants take an intermediate position as regards incidence. Usually the growth arises in the substance of the gland fairly close to the nipple, but occasionally an outlying lobule is affected first. In the axillary prolongation of the breast a tumour may be mistaken for an enlarged lymph gland. Rarely both breasts are

affected simultaneously or in succession—a remarkable exception to the general rule, which suggests that cancer may depend upon some

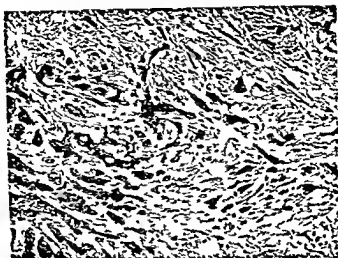


FIG 1-1 Scirrhous carcinoma of the breast. Invading columns of malignant cells surrounded by a dense stroma of fibrous tissue

general upset of cellular activity as well as upon a local growth perversion

Characteristically, the tumour is of small size, and is stony hard

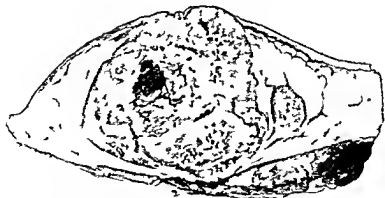


FIG 1-2 Encephaloid cancer of the breast. The tumour is of large size and has undergone extensive necrosis with the formation of a spurious cyst. It has invaded the pectoral muscle and has begun to ulcerate at the skin surface

(Department of Surgery University of Edinburgh)

so that it is most evident when the breast is pressed by the flat of the hand against the chest wall. From the first it is firmly fixed within the breast substance, and later, from contraction of its tough fibrous stroma, it pulls upon surrounding structures. When the tumour is related to the larger milk ducts it may cause some elevation and fixity of the

nipple at quite an early period. Later the nipple becomes deeply retracted. By traction exerted upon the ligaments of Cooper the skin over the tumour may become dimpled, and later adherent. Eventually the tumour becomes fixed and immobile upon the chest wall, and it may ulcerate through the skin surface.

When the breast is cut, the nature of the tumour is usually obvious. It is so hard that the tumour may creak in the process and impart an almost gritty sensation. In the bisected breast the tumour is seen to be of small size, but invading the breast in all directions and it has no capsule. It is fibrous, light grey or pinkish grey in colour, and it retracts somewhat when cut, so that the cut surface becomes slightly concave. Scattered through the tumour there are often pale fibrous streaks and pin head yellow spots of necrotic epithelial tissue, so that the appearance is aptly comparable to the cut surface of an unripe pear.

Microscopically, the tumour is composed of spheroidal epithelial cells in a stroma of fibrous tissue. The spheroidal cells are believed to be derived from ductal epithelium, but they exhibit no glandular arrangement and he simply in solid masses or in

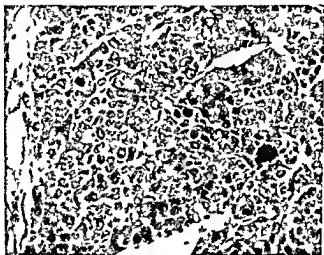


FIG. 173. Acute lactation cancer of the breast  $\times 300$ . The tumour is one of great malignancy. The cells are of primitive character, and there are numerous mitotic figures. A malignant giant cell is present.

(Laboratory of Royal College of Physicians of Edinburgh.)

finger like columns which invade the surrounding tissues in all directions. The stroma is present in abundance and is composed of tough fibrous tissue, hence the hard or scirrhus nature of the tumour. The elastic lamina of the ducts shows striking (and unexplained) overgrowth. Often towards the periphery of the tumour, however, the stroma is less dense and the epithelial cells are present in greater numbers, as though more vigorous and invasive in this region. In such places the microscopic appearance may resemble that of an "encephaloid" tumour.

The atrophic scirrhus cancer is an extreme variety of the ordinary form. It is found in atrophic breasts, and especially in women over the age of sixty five, and it forms a tumour of very slow growth and low malignancy.

The breast is shrunken, the nipple deeply retracted, and the skin over the tumour deeply puckered. The tumour is small, but very hard and fibrous, and is firmly adherent. Metastases develop only after a

long period, and death may be delayed for as long as fifteen years. Microscopically there are small islands and delicate strands of spheroidal epithelial cells embedded in dense fibrous tissue.

The Medullary (Encephaloid) Carcinoma has the same essential nature as the scirrhous variety, but it is softer, more cellular, and more rapid in growth and dissemination. It occurs typically in well-developed breasts in younger women, and forms a large soft mass that infiltrates widely. When cut, it is of spongy texture, or almost brainlike and hemorrhages and large areas of necrosis are common. Microscopically it is composed of solid masses of epithelial cells supported in a delicate connective-tissue stroma. The epithelial cells are spheroidal or sometimes almost columnar and may show mitotic figures and other evidence of rapid division. The tumour is often vascular and the vessels are thin walled, and bleed readily.

The acute cancer of pregnancy and lactation represents an extreme form of the encephaloid type. It is a highly malignant tumour which grows rapidly to large size, and leads to an early fatal issue, often in the course of a few months. The breast becomes diffusely swollen and painful and dilated veins appear under the skin. The tumour is very vascular and since there is already a state of physiological hyperæmia the whole breast becomes hot. A slight rise in body temperature may be observed with impairment of appetite and malaise and consequently the tumour may be mistaken for a deep-seated abscess and incised.

On cross section the tumour presents a soft hemorrhagic, infiltrating mass often with large areas of necrosis. Microscopically the epithelial cells show every sign of extreme malignancy. Mitotic figures of irregular pattern are common, nuclei stain deeply, and the cells vary greatly in size and shape. The anaplasia may be so great that the tumour resembles a sarcoma.

It should be mentioned that a mammary carcinoma arising in pregnancy or lactation does not invariably progress so rapidly. A moderately prolonged survival after operation is not rare.

**Adenocarcinoma.** This title was used by Halsted to describe mammary tumours containing large tubular spaces lined with many layers of epithelial cells. It is now applied to a tumour in which the cells are not entirely arranged in solid masses but exhibit in places a glandular arrangement. In most cases a tumour of this class approximates to a localized form of intraductal malignant hyperplasia (*see p. 380*) and is consequently of low-grade malignancy. Some such tumours are partly composed of large clear rounded cells resembling sweat gland cells. They have been described as "sweat-gland carcinoma" and have been regarded as arising from sweat-gland rests isolated during development (Creighton). In Dawson's opinion, on the contrary, the tumours are derived from the ordinary epithelial cells of the breast, and the pale appearance of the cells results from degenerative changes. It is possible that other adenocarcinomata arise from the malignant transformation of papillomata in ducts and cysts.

**Mucoid Carcinoma (Colloid or Gelatinous Carcinoma).** Small areas of mucoid degeneration are not uncommon in mammary growths and



occasionally this change is sufficiently obvious to merit separate description. In well marked examples a large area or even the entire tumour



FIG 174 Mucoid (colloid) cancer of the breast. The tumour is an adenocarcinoma that has undergone mucoid change and it contains numerous cystic spaces filled with jelly like material. Though massive it is fairly well circumscribed and not very malignant.  
(Department of Surgery, University of Edinburgh)

is affected. The mucoid material is a product of the malignant epithelial cells. At first it lies within the cells which as a consequence become distended to signet ring shape. Later the mucoid material is set free in the intercellular stroma sometimes in such large quantities as to obscure the small and more or less degenerated epithelial cells.

Mucoid cancers are usually bulky and of soft consistency, but their apparent malignancy is usually belied by slow growth and late dissemination. Occasionally, however, they are rapidly invasive.

When cut, the tumour is seen to be



FIG 175 Mucoid cancer of the breast  $\times 80$ . Small collections of spheroidal epithelial cells are surrounded by masses of mucoid (colloid) material.  
(Laboratory of Royal College of Physicians of Edinburgh)

composed mainly of soft, jelly like material, yellow or red in colour often collected in cyst like spaces. In places there are masses or streaks of solid tumour tissue of pale colour. Microscopically, there is sometimes difficulty in recognizing the nature of the tumour, for many of the epithelial cells are degenerate, and are scattered as small islands in homogeneous jelly like areas of mucinous substance.

### CARCINOMA OF THE MALE BREAST

Cancer of the male breast is rare, no doubt for the reason that it is exempt from the physiological stresses to which the female breast is subject. It is significant that gynecomastia is present in a considerable proportion of cases. In general character the tumours correspond to those of the female breast and they are usually of slow growing scirrhus type. Most cases occur between the ages of fifty and sixty years. Not infrequently the breast has been subjected to constant or repeated trauma often occupational—for example, by the pressure of a bootmaker's last. Rarely the carcinoma takes origin in a simple tumour of long duration. Since the male breast is of small dimension the tumour early transgresses its limits and invades the pectoral muscles the skin and the lymph glands. This early spread, together with the technical difficulty at operation of excising a sufficiently wide margin of healthy tissue from the thinly clad male thorax, renders the prognosis somewhat more grave than in the female.

### SPREAD OF CARCINOMA OF THE BREAST

The methods and routes of spread of carcinoma of the breast have been the subject of prolific research and much well-established information has resulted. The pathological and surgical importance of the subject requires no emphasis.

**Spread via Lymph Vessels.** This is by far the most important route for dissemination in cancer of the breast, just as it is in any other carcinoma.

The actual mode of lymph vascular dissemination remains a controversial subject. According to Handley's theory of lymphatic permeation, the growing neoplasm permeates surrounding tissues in delicate invading columns which extend by a continuous multiplication of its advancing cells. This invasion takes place radially in all directions, whether in the direction of the normal flow of lymph or against it. As the rapidly growing cells at the head of each column progress the cells further back undergo degeneration as a result of reactive fibrosis so that, while the peripheral growth extends the more centrally placed portions are obliterated. Thus there is formed a more or less circular zone of actively progressing malignant disease, a "neoplastic ringworm," which gradually increases in diameter and tends to form secondary nodules in skin, bones and viscera at progressively greater distances from the primary growth.

Handley has offered a mass of interesting evidence in support of this theory. He has emphasized that the earliest metastatic nodules in

the skin are found close to the breast or in the sear of operation, whereas later the skin further distant may be involved. Similarly, metastases in bone, he claims, occur first in the ribs, sternum and vertebræ, later in the upper ends of the humerus or the femur, and rarely at more distant situations. Furthermore, metastases in bone occur most often on the same side as the primary growth. The upper end of the femur, for instance, is involved three times more commonly on the same side as the primary tumour than on the opposite side.

In recent years, however, the permeation theory has suffered contradictions. Microscopically, it is usually impossible to demonstrate evidence of destruction of malignant cells and obliteration of lymph vessels within the spreading circle, and on the contrary the tissues close to a primary growth are usually more heavily infiltrated with malignant cells than those more distant. Comparison with the mode of spread of carcinoma elsewhere, *e.g.*, in the tongue, does not support Handley's hypothesis.

It is now generally believed that extension *via* the lymph vessels depends principally upon a process of embolism, cancer cells or masses of cells being detached from the parent growth and set free in the lymph stream. They are carried first along the periductal lymph vessels to the subareolar lymph plexus (Sappey) or to the extensive plexus of lymph vessels in relation to the deep fascia. Thence they are carried to the regional lymph glands. In the early stages the most important dissemination is to the axillary glands. "Leaf's gland," close to the axillary tail of the breast, and the pectoral group of axillary glands are usually affected first. From these there is extension to other groups of axillary glands and later through the apex of the axilla to the supraclavicular glands. Occasionally the primary tumour spreads directly to glands of the apical group by lymph vessels that penetrate the greater pectoral muscle and the costo coracoid membrane. The small collection of glands in the infraclavicular triangle may be infected by the same route.

A growth in the medial half of the breast often disseminates early to the glands situated along the internal mammary artery, and these in turn readily infect the mediastinal glands, the pleura and lung.

Tumours in the lower medial quadrant of the breast are situated, as Stiles pointed out, immediately superficial to the sheath of the rectus muscle, and not far distant from the epigastrium, so that dissemination *via* this "dangerous angle" is relatively frequent. The peritoneum may be invaded by malignant cells, which form either multiple small scattered deposits or a few large masses in the omentum or on the pelvic floor. The liver, often the first viscus to be affected, may be invaded from its peritoneal surface, and is usually riddled with deposits.

In advanced cases, and rather uncommonly, the disease may spread by lymph channels across the mid line, to affect the opposite breast or its axillary glands.

**Involvement of Skin.** The skin may be affected in several ways, either by malignant invasion or as a secondary result of obstruction of lymph vessels in the corium.

(1) Direct invasion is particularly apt to occur if the primary

tumour is situated superficially. The overlying skin is thinned and later ulcerates. In the scirrhus varieties of tumour the ulcer may resemble a squamous cell carcinoma, with indurated, rolled edge and a raised sloughing base. More bulky tumours tend rather to project as soft, fungating, often hæmorrhagic masses.

(2) Multiple metastatic nodules may appear around the tumour, either in a healthy area of skin or in parts modified by lymph vascular obstruction. At first, they tend to appear close to the primary tumour or, after operation, in or close to the scar, later, they may extend to cover large areas of the thorax and abdomen. According to Handley, the nodules result from the invasion of the skin from below, by cells derived from the growing edge of the annular zone of permeation along the deep fascia.

(3) *Peau d'orange*. In this affection the skin becomes tense, thickened and œdematous, not from true cancerous invasion but from obstruction of deep lymph channels by the malignant growth. The tiny pitted depressions that mark the site of hair follicles and sweat glands give the appearance of pigskin or orange peel.

(4) *Cancer en Cuirasse*. *Cancerous Pachydermia*. This is a curious condition of the skin occurring, somewhat rarely, in the late stages of the disease, and especially in relation to a carcinoma of a slow growing scirrhus type. The first change is a retraction of the skin immediately superficial to the growth, which becomes fixed and indurated. The change progresses until it may affect the greater part of the thoracic and abdominal surface. The arm of the same side is almost invariably affected, the opposite one not infrequently. The affected skin is at first thick and œdematous, pitting on pressure. Later, it becomes shrunk, tense, and as hard as leather, so that eventually the trunk is enclosed in a semi rigid case which may be so tightly stretched as to interfere with respiration. Scattered over the affected skin there are often secondary cancerous nodules which may be pale, pigmented or hæmorrhagic. "*Cancer en cuirasse*" is believed by some to arise from a widespread infiltration of the skin by a very scirrhus growth. Others regard it as secondary to the œdema of lymphatic obstruction.

**Dissemination to Bones.** It has already been remarked that metastatic deposits in bone occur most frequently in the vertebral column, less often in the upper ends of the humerus and the femur and the skull, and only rarely in more distant situations. Handley claimed that this distribution is clear confirmation of the method of spread by lymph vascular permeation. Pincey, however, believes that it can be explained on the basis that all these regions in the bones normally contain red bone marrow, and that blood borne cancer cells grow most readily in this tissue. The first sign of a metastasis in bone is found in the centre of the marrow, with no trace of invading columns of cells between it and the periosteum. Similarly a metastasis in the cranial bones always commences in the diploe.

**Dissemination by the Blood Stream.** In addition to the secondary deposits in bone, it is generally believed that a certain number of other metastatic growths, especially in the lungs and brain, arise from emboli disseminated by the blood stream. Schmidt showed, many years ago

that such emboli can be demonstrated frequently in the pulmonary vessels at the time of death, and although, as he believed, many of these are walled off by a protective sheath of blood clot, it seems likely that some few may engraft on the wall of the vessel and produce a secondary growth

### SARCOMA

The activities of the breast are related principally to its epithelial elements, and it is therefore not surprising that connective tissue tumours are much rarer than carcinoma

Sarcoma accounts for under 3% of all mammary tumours. It may arise *de novo* in the breast, and is then either of spindle cell or round cell type, or it may represent a malignant change in a pre-existing fibro adenoma of the intracanalicular type (adeno sarcoma). In this latter variety both ectodermal and mesodermal elements are present, and the spindle cells, large or small, may be arranged around ducts or spread diffusely. The two types are distinguishable clinically only by the longer history of the latter variety. Both form rapidly growing massive fleshy tumours, which infiltrate the breast, and lead to metastases in the lungs or other viscera

### RARE TUMOURS IN THE BREAST

*Teratoma* is of rare occurrence in man, though common in dogs. Islands of cartilage, calcified areas, and sometimes bone are found scattered through a stroma of spindle cells. The tumour is usually malignant and resembles sarcoma in its course. Its chief interest lies in its origin. It probably arises in the same way as similar tumours in the mediastinum from displaced totipotential cells.

*Squamous cell carcinoma* may arise from the skin, the areola or the terminal portions of the milk ducts. *Melanoma* and *malignant angioma* have been described.

### TRAUMATIC FAT NECROSIS

This is an affection of adipose tissue which is especially apt to occur in the neighbourhood of the breasts, particularly in obese women. It is in no sense an affection of the mammary gland, but as it is apt to be mistaken for carcinoma, it may conveniently be considered here.

The disease was first recognized in 1896 by Shattock, who described an example occurring in relation to a lipoma in the buttock, and the name, "traumatic fat necrosis," was assigned to it by Lanz in 1898.

In about 50% of cases the lesion follows some known injury, either a blow or, not infrequently, the trauma associated with subcutaneous administration of saline solution. It is possible that in the remainder the causative factor is some minor but oft repeated trauma such as may result from the pressure of clothing or the drag of a heavy, pendulous breast. A few weeks after the injury, or occasionally much later, a lump develops in the breast or in the subcutaneous tissue close to it. The lump is circumscribed and is of stony hardness and adherent to the breast and surrounding tissues. In about half the

cases the skin overlying it is tacked down and sometimes there is a pigskin appearance like that in cancer. Occasionally the nipple is retracted.

When cut, the lump is seen to be composed of tough fibrous tissue, in the centre of which are pale chalk like areas and spaces containing liquefied fat. It may be distinguished from cancer by the absence of the characteristic small yellow spots of epithelial debris, and by the obvious lack of infiltration.

The essential pathological feature is a slow aseptic saponification of neutral fat. In the centre, fat is liquefied, and around it the products of saponification excite a foreign body reaction. Microscopically, globules of fat, fatty acid crystals and sometimes calcium deposits are evident at the centre, and around them is a large mass of fibroblastic tissue. Many phagocytic cells are seen filled with fat globules and usually there are numerous giant cells of the foreign body type.

### PAGET'S DISEASE OF THE NIPPLE

This is a rare disease of middle aged and elderly women characterized by an eczematous affection of the nipple, which coexists with or is followed by a carcinoma in the breast. The condition begins at the

nipple, which assumes a bright red, florid, finely granular surface, well defined at its margins, and covered by dry scales or exuding a clear or sanguineous discharge. The lesion is slowly progressive, over a period of months or years eventually eroding the nipple and covering the areola and the surrounding skin over an area which may attain a diameter of 4 or 5 cm.

Microscopically, there are several characteristic changes both in the epidermis and in the true skin.

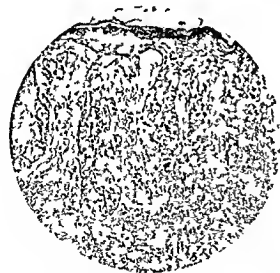


FIG 176 Paget's disease of the nipple  $\times 80$ . The inter papillary processes of the epidermis are enlarged and contain the typical Paget's cells. There is a lymphocytic infiltration of the corium.

(Laboratory of Royal College of Physicians of Edinburgh)

(1) The epidermis, ulcerated superficially, at the same time undergoes proliferative changes, which become evident on its deep aspect, where the inter papillary processes become increased in depth and in breadth (see Fig 176).

(2) The most characteristic feature is the occurrence of "Paget's cells," which lie singly or in small groups in the deeper parts of the epidermis, especially in the prickle-cell layer. The cells are at first large and rounded, with the appearance of cells of an undifferentiated glandular carcinoma, but they rapidly undergo retrogressive changes and assume a hydropic, degenerated appearance (see Fig. 177).

(3) Coincidentally there are changes in the true skin. Collections of lymphocytes and plasma cells appear in the papillæ of the corium, the capillaries may be dilated, and there is often a fibroblastic reaction. These changes are believed by some to precede the epidermal lesions and to be important features of the whole process. Others regard them as the results of an almost inevitable mild infection of the free surface.

(4) Along with these lesions at the nipple there are almost always proliferative changes in the underlying breast. The ducts are dilated or cystic, and various degrees of epithelial hyperplasia may be present.

**Ætiology.** The nature of the disease has been the subject of much controversy, and still remains unsolved. Particular interest attaches to its relationship to the underlying carcinoma. A subjacent carcinoma almost invariably occurs, sometimes shortly after the appearance of the affection of the nipple, usually within two years, but occasionally as long as ten or even twenty years later. The tumour, which is usually of the slow growing, scirrhus variety, may arise in any part of the breast, and may be at some distance from the nipple.

According to Handley, the nipple lesion is due to oedema of the epidermis resulting from obstruction of the lymphatics by the deep seated carcinoma.

The theory more widely accepted is that propounded by Muir. Muir emphasizes that in every breast affected by Paget's disease examined by him there has been present a wide spread hyperplasia of the epithelium lining the ducts—the con-



FIG. 177. Paget's disease of the nipple.  $\times 175$ . The section shows two intercapillary processes of the epidermis containing numerous Paget cells. Note the lymphocytic infiltration in the corium.

(Laboratory of Royal College of Physicians of Edinburgh.)

dition he describes as "introduce cancer" (p. 380). This hyperplasia is the primary factor which leads to the development both of the nipple lesion and also of the underlying scirrhus carcinoma.

According to this theory, hyperplastic epithelial cells derived from the milk ducts close to the nipple invade the epidermis and lead to the ulcerative lesion in that area. These invading cells form the "Paget cells," and their peculiar hydropic appearance is due to degenerative change induced by the reaction of the epidermis.

Similarly, hyperplastic epithelial cells in one of the ducts deep in the breast may also assume invasive characters, penetrate the duct wall and give rise to the formation of a scirrhous carcinoma.

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## CHAPTER XIX

### DISEASES OF THE MOUTH, JAWS, SALIVARY GLANDS AND NECK

#### DISEASES OF THE LIPS

##### *Carcinoma*

CARCINOMA of the lip is a common condition which arises most often between the ages of fifty and seventy years. In over 90% of cases the male sex is affected, and in a similar proportion the growth is situated on the lower lip, especially at a point between the midline and the angle of the mouth.

Carcinoma of the lip is commonest in countrymen, especially those exposed continuously to sunlight. It is generally believed that the common predisposing factor is chronic irritation and hyperplasia consequent on the use of a hot tobacco pipe, especially of the short clay variety. This habit explains the common situation and incidence of the growth. In this connexion it is interesting to observe that in women the disease is almost confined to pipe smokers. Whilst the ætiological significance of pipe smoking is generally assumed, it is not accepted by all authorities, and Broders, in particular, has maintained that the relationship is more apparent than real. Lane Claypon moreover, has shown that statistically there is no support for the belief that smoking as such, has any definite relationship to cancer of the lip, though it is conceded that the heat of a pipe stem or the excoriation induced by cigarette paper may be predisposing factors. In some cases a syphilitic lesion, a wart or fissure or patch of leucoplakia, seems to be a predisposing factor.

Occasionally a growth on the lower lip is accompanied by one in a corresponding position on the upper lip, an occurrence usually attributed to implantation of free malignant cells on the opposed surface.

**Naked-eye Appearance.** The carcinoma may at its onset take one of several forms, generally it appears as a small warty growth on the surface of the lip, accompanied by a button like induration of the subjacent tissue. Less often it appears as a fissure which fails to heal and becomes indurated. Yet again it may be ulcerated from the start and form a small erosion which crusts over but persists and enlarges.

Later in its course the growth may assume either of two forms, the papillary and the ulcerative. (1) *The papillary form* has the appearance of a wart like thickening, elevated above the surface. It extends slowly with little surrounding infiltration, and it is slow to invade the deeper structures. Eventually it ulcerates and then follows the usual course of the second form. (2) *The ulcerating form* is more common. It has the appearance of a typical malignant ulcer, with a raised, irregular, rolled margin and a red, indurated base.

deeper tissues until it has extended superficially beyond the lupus area and has thus reached permeable lymph vessels. It then takes the usual course of skin carcinoma and metastasizes to regional lymph glands.

Basal-cell carcinoma is another lesion of the face that is liable to malignancy, though rarely. Sometimes the stimulus of inadequate irradiation by X rays or radium has appeared to determine this change. In other cases long-continued irritation by carcinogenic paraffin products forms the predisposing factor, and in shale oil workers and mule spinners the face is a not uncommon site for skin carcinoma (*see p 71*). Rarely a carcinoma has followed the irritation of tar products, and a case has been reported in which carcinoma has occurred within a few months at a point burnt by a single spurt of hot tar.

## DISEASES OF THE TONGUE

### Leukoplakia (Chronic Superficial Glossitis)

This is a chronic affection of the tongue characterized by patchy clumping of the epithelium with atrophy of the papillæ and chronic inflammatory changes in the subjacent dermis. It is of importance as an intractable form of hyperplasia which shows a definite tendency towards cancerous change.

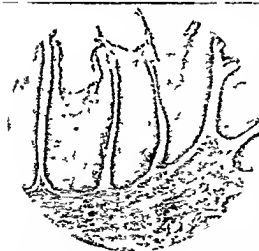


FIG 181 Leukoplakia of the tongue. There is very considerable proliferation of the middle layer of the epidermis, with keratinization on the surface. The basal layer of cells is little affected.

The patches of leukoplakia vary in size, and, in extreme cases, may cover the greater part of the tongue. They usually begin near the lateral edge of the tongue in its anterior two-thirds, and spread thence on to the dorsum, or sometimes to the floor of the mouth. Rarely they occur on the lingual aspect of the cheek, and on the lips or gums.

In the affected area the mucous membrane is somewhat indurated, slightly raised above the general surface, and of a

greyish white colour, as though coated with paint. The lingual papillæ are flattened and atrophied, and may participate in the patchy whiteness. In advanced cases, a different appearance is sometimes seen. The superficial layer of the epidermis disappears, and the patchy whiteness gives place to a diffuse red appearance sometimes compared

to raw beef. When the leukoplakia is extensive and of old standing the tongue becomes fissured.

Microscopically, there are pathological changes in both the dermis and the epidermis. The dermis is the seat of a chronic inflammatory reaction, is unduly vascular and oedematous, and is infiltrated with small round cells of lymphocyte type.

The epidermis presents histological changes affecting any or all of its various layers. The most striking deviation from normal is seen in the cells of the middle layers of the epidermis, which are swollen, vacuolated, and in some parts loaded with eleidin granules. In some cases there are collections of large hydropic cells, which somewhat resemble the characteristic cells of Paget's disease of the nipple (see p. 390). As a result of these changes in the middle layers the epidermis increases in thickness, and the interpapillary processes become broader and project more deeply towards the corium.

The superficial layer of the epidermis is generally increased in depth, keratinization is a prominent feature, and the superficial cells are extensively cornified. It is this feature that is responsible for the patchy whiteness of leukoplakia. In other cases, especially in the late stages of the disease, the superficial layers are reduced in depth or even absent.

The basal layer of the epidermis also shares in the proliferative changes of leukoplakia. The basal cells are hyperplastic, their nuclei are hyperchromatic and show some variability of size, and their cytoplasm is less granular and often somewhat swollen. In some cases, the basal cells present a degree of hyperplasia approximating to malignancy, and indeed the distinction between extensive leukoplakia and early malignancy is by no means easy.

In the late stages of leukoplakia, when the tongue presents the raw beef appearance, the microscopic features are different. The epidermis is now considerably thinned, and represented only by the basal cells, the superficial layers having been eroded. The basal cells are still more irregular in shape and size, and in their staining reactions they may show all the features of malignancy.

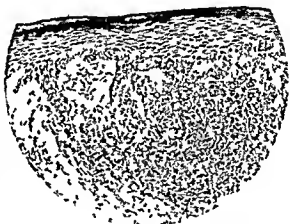


FIG. 182. Leukoplakia of the tongue. The basal layer of the epidermis is markedly hyperplastic. The more superficial layers are relatively unaffected. Note the extensive lymphocytic infiltration of the dermis.

**Ætiology of Leukoplakia.** Leukoplakia is rare before the age of thirty years, and is most common between the ages of forty and fifty years. It affects males far more often than females.

The Wassermann reaction is positive in more than 50% of cases, and it is generally believed that syphilis is an important predisposing cause.

Leukoplakia occurs most commonly in pipe smokers. It is not certain whether the heat of the tobacco smoke or the action of irritant combustion products is responsible.

In some cases irregular teeth or badly fitting dentures may be incriminated. Recent observations suggest that the presence of multiple dental fillings composed of dissimilar metals may play a part in the ætiology, by setting up minute electrical currents when touched by the tongue. In this connexion it is interesting to note that Fitzwilliams has recorded a case of an electrician, who developed two small patches of leukoplakia, possibly due to repeated electrical stimulation when testing batteries by contact with the tongue.

Finally, it has been suggested that deficiency of vitamin A, which is known to impair the nutrition of epithelial tissues, may be a significant factor.

In regard to the pathological changes in leukoplakia, there are two main views. The commonly accepted view is that the primary change is proliferation affecting the basal cells of the epidermis, that the modifications in character of the superficial cells are secondary to this, and that the changes in the corium are of a reactive nature or due to superadded inflammatory processes.

The opposing view, which has been supported recently by Mehie, is that the initial lesion is a chronic inflammation, possibly toxic in origin, which primarily involves the subepithelial tissues, and later, as a result of œdema and vascular changes, affects the nutrition of the epidermis and leads to proliferative changes in that membrane.

### Syphilis of the Tongue

The tongue may be affected by syphilis, either inherited or acquired. It is one of the commonest sites of extra genital chancre, it regularly participates in the secondary manifestations, and it is often involved in lesions of the tertiary stage.

The primary lesion, or chancre, results from a direct infection, and consequently is commonest close to the tip of the tongue. The chancre forms a hard indolent nodule which ulcerates at an early stage and follows a course similar to that in other situations. It is accompanied by considerable enlargement and tenderness of the regional lymph glands in the submandibular and submental regions.

Secondary syphilitic lesions of the tongue usually take the form of mucous patches. They are most evident on the back and sides of the tongue, and are usually accompanied by similar lesions on the fauces, tonsils and palate.

Tertiary syphilitic lesions of the tongue are of especial interest from their relation to earenuma. Three distinct forms may be

recognized (1) chronic superficial glossitis (leukoplakia), (2) chronic parenchymatous glossitis, (3) gumma of the tongue

(1) Chronic superficial glossitis in syphilis is characterized by changes in the superficial parts of the dermis and in the epidermis. An infiltration of round cells is succeeded by fibrosis in the dermis, and at the same time the epidermis presents the changes characteristic of leukoplakia.

(2) Chronic parenchymatous glossitis may be regarded as a diffuse gummatous infiltration of the tongue, and it is a common occurrence in tertiary syphilis. A similar but non-syphilitic glossitis may occur in a mercury stomatitis, and occasionally from other causes.

The essential pathological feature is an infiltration of the connective tissues and muscles by small round cells of lymphocyte type, which is followed by connective tissue proliferation and, later, by fibrosis. In the early stages the tongue is swollen, and may be ulcerated. Later it becomes shrunken and distorted, lobulated like a cirrhotic liver, fissured and indurated.

(3) Gumma of the tongue occurs usually as a late tertiary phenomenon. It may be single or multiple. Multiple gummata are usually of small size and situated near the surface of the tongue, whereas a solitary gumma tends to attain greater dimensions and to arise more deeply.

A solitary gumma almost always lies in or close to the midline. At first it is deeply placed and forms a globular swelling of hard consistency. It increases in size somewhat rapidly, and later breaks down on the dorsal surface of the tongue, forming a chronic ulcer, deeply excavated, with hyperemic, undermined or sharply cut margins and a yellow sloughing centre or base. A gumma is usually painless, and causes little interference with comfort or function. The ulcer is surrounded by little or no induration in the substance of the tongue, and its edge unlike that of a carcinoma, is not raised, rolled or thickened.

### Carcinoma of the Tongue and Mouth

Carcinoma of the tongue is a new growth of common occurrence. In England and Wales it is responsible for approximately a thousand deaths annually. It occurs most often between the ages of forty-five and sixty years, but is common at later ages, and is not unknown as early as the thirtieth year. Males are affected in 90% of cases, an incidence once attributed to the greater frequency of syphilis and smoking.

The predisposing factors in carcinoma of the tongue may be said to include all agents which result in an irritative hyperplasia of the mucous membrane. Syphilis is said to coexist in from 50% to 80% of cases in which the dorsum of the tongue is involved. It probably exercises a predisposing influence through the fissuring, scarring and leukoplakia to which it gives rise. Non-syphilitic forms of leukoplakia precede the carcinoma in an appreciable proportion of cases. In other instances recurring trauma from sharp teeth or dentures, infection from pyorrhœa and irritation from hot tobacco smoke may be incriminated. It is noteworthy that carcinoma of the tongue is rare in the eden-

tulous, and that it occurs usually at the side of the tongue where irregular teeth and the irritation of pipe smoking may be supposed to have the greatest effect.

In certain parts of India the practice of chewing calcareous matter flavoured with betel nut is well known to predispose to cancer, and in other parts of the world tobacco chewing is said to have the same effect. This form of cancer is especially apt to occur inside the cheek at the point where the bolus is lodged.

**Site Affected.** In most cases the carcinoma arises at or near the edge of the tongue in its anterior two-thirds, or at a corresponding level in the floor of the mouth. Carcinoma near the midline of the tongue is uncommon, and almost invariably secondary to a syphilitic



FIG. 153. Cancer of the tongue. Note the small ulcer and the raised, indurated margin. The tumour is unusually close to the mesial plane and has caused less fixation of the tongue than is usual.

(Museum of Royal College of Surgeons of Edinburgh.)

lesion. The tip of the tongue is rarely involved. Carcinoma in the posterior part of the tongue occurs commonly at the side close to the glosso-palatine arch. The posterior part of the tongue may be invaded by carcinoma of the epiglottis and pharynx.

**Naked-eye Appearance.** The appearance of the growth is usually characteristic, and such atypical forms as are described are rare. In its early stages the growth may take the form of a hard submucous nodule (nodular type), a large, red, projecting papillomatous mass (papillary type), or a deep fissure with indurated margins (fissured type). In the majority of cases, however, whatever the manner



FIG. 154. Carcinoma of the tongue. The growth has originated at the under surface of the tongue and has infiltrated the floor of the mouth and the mandible.

(Museum of Royal College of Surgeons of Edinburgh.)

of its origin, the growth rapidly breaks down and forms a malignant ulcer (ulcerative type). Such an ulcer on the tongue has a highly characteristic appearance. The actual crater is not necessarily deep, and may be of small size. The floor of the ulcer is of irregular shape, and is surrounded by a broad margin, which is raised, nodular and everted.

The base of the growth and the adjacent substance of the tongue are indurated and of stony hardness

Rarely the tumour does not ulcerate, but spreads deeply and infiltrates the root of the tongue, causing it to become indurated, puckered and shrunken (*wooden tongue*)

**Microscopic Appearance** In the great majority of cases the growth is a squamous cell carcinoma (*epithelioma*) Carcinoma of basal cell type occurs less commonly Adeno carcinoma has been described, but is extremely rare The ordinary squamous cell carcinoma has the characteristics common to tumours of this type, and consists of clubbed or flask shaped processes of epidermis which grow down into the subjacent stroma and muscle The majority of the cells are of the character of prickle cells According to the degree of malignancy there are varying degrees of anaplasia, and in the more rapidly growing tumours mitotic figures are numerous Cell nests are sometimes present but are not invariable

**Effects** The malignant ulcer is prone to bleed and liable to gross secondary infection, and such complications bring the patient to a state of anæmia and cachexia The breath is foul and foetid Infiltration of the muscles leads to fixation of the tongue and to interference with articulation and deglutition The tongue is protruded with difficulty, and tends to deviate towards the affected side Salivation is increased, and since deglutition is painful saliva dribbles from the mouth

Pain is an early symptom, and may be so severe as to interfere with sleep At first the pain is limited to the affected region, but later it radiates through the tongue, and eventually, by reflex involvement of the chorda tympani and the auriculo temporal branch of the trigeminal, it is referred to the ear and the side of the face and head

**Spread** A carcinoma of the tongue spreads locally and invades regional lymph glands The floor of the mouth and the muscles at the base of the tongue are involved early, and if the tumour is situated far back it may spread to the tonsil, the palatine arches and the palate The lymph glands involved first are usually those of the submandibular (submaxillary) group The submaxillary salivary gland frequently escapes The glands of the upper deep cervical group are generally involved later, but sometimes they may be the first to be obviously enlarged, especially from a growth in the posterior part of the tongue. From the tip of the tongue the submental glands are often involved at an early stage

Spread to distant situations such as the mediastinal lymph glands the liver and the lungs is uncommon, except in the later stages, and death is usually the result of such local complications as hæmorrhage, infection and bronchopneumonia

### Rare Tumours of the Tongue

Occasionally the tongue becomes the seat of sarcoma In the majority of cases it is a lymphosarcoma derived from the lymphoid tissue on the posterior third of the tongue The tongue may be involved in lymphosarcoma derived from the tonsil Rarely a spindle-

cell and mixed cell sarcoma occurs. Such tumours present no special characteristics. They form soft rounded masses, which grow rapidly and are prone to hæmorrhage and infection. Metastases may occur in distant situations, but usually death is due to sepsis or hæmorrhage from the vascular tumour.

Other rare tumours of the tongue include lymphangioma, cavernous angioma, papilloma, fibroma, lipoma, osteoma, rhabdomyoma, mixed tumours and ectopic thyroid enlargements (*see p. 420*).

### Tumours of the Palate

The commonest tumour of the palate is the *squamous cell carcinoma* (epithelioma), and it may originate in this situation or spread thither from the alveolus or cheek. It forms an ulcerating tumour which has the general characteristics of such growths and spreads slowly, involving neighbouring tissues and metastasizing to regional lymph glands.

A *sarcoma* affecting the palate usually originates in the maxilla in the region of the antrum.

*Mixed cell tumours* occur in young subjects and are similar in structure to salivary gland tumours. In some cases striped muscle fibres have been present (rhabdomyoma). Such tumours vary greatly in malignancy, but usually they are of rapid growth.

*Endothelioma*, *adenoma* and *papilloma* are extremely rare.

### Lympho-Epithelioma of Nasopharynx

This is a tumour in which lymphoid tissue is intimately associated with an immature squamous or epidermoid type of malignant epithelium. It arises in the nasopharyngeal mucosa and in the faucial, lingual and pharyngeal tonsils. The epithelial element consists of squamous cells in solid strands with no pearl formation and no cornification. Lymphocytes occupy the supporting tissue and may penetrate between the epithelial cells.

The tumour forms a soft fungating mass which grows rapidly, ulcerates and bleeds. It metastasizes early to lymph glands in the neck and occasionally to distant sites such as the mediastinal glands, bones and viscera. If untreated it generally proves fatal within two years. Radiotherapy produces remarkable, though transitory, regression.

The true nature of the tumour is obscure. It is regarded by some authorities as a true mixed tumour, with a peculiar and intimate relation between the epithelial and lymphoid components. It must be remembered however, that lymphoid aggregations occur normally in close proximity to the epithelium in the tonsils and nasopharynx, as indeed also in other parts of the alimentary tract such as the appendix, and that lymphocytic infiltration of the stroma is a regular feature of undoubted carcinoma in these regions. In view of this association, some observers regard lympho-epithelioma merely as a form of carcinoma in which the lymphoid tissue maintains its original relation to the epithelium.



## CYSTIC SWELLINGS OF THE MOUTH

Small retention cysts may occur in the mucous glands of the lips and cheeks, and if they are situated near the teeth they may become abraded and ulcerated. Cysts of a similar nature may also occur along the edges of the tongue and in the glands (of Blandin and Nuhn) situated beneath the tip of the tongue.

These cysts are of a bluish grey colour, small in size, very thin walled and well circumscribed. Their contents are thin, clear and jelly like.

**Ranula.** This is a conglomerate term applied to cystic swellings in the floor of the mouth. The exact nature and origin of some of these cysts are not entirely established.

The cyst is usually unilateral, but it may be bilateral. It generally appears in childhood, and grows slowly. It is bluish grey in colour and situated at the side of the frenum. The mucous membrane over the cyst is thin but movable. The tongue is raised to a variable extent according to the size of the mass, which may be several centimetres in diameter. Sometimes the cyst extends behind the mylohyoid muscle and causes bulging in the neck behind the submaxillary gland. The duct of the submaxillary salivary gland is separate from the cyst. Occasionally a cystic tumour of the floor of the mouth has a communication with a cyst in the neck, and pressure on the oral swelling increases the size of that in the neck. A large cyst of long standing may cause pressure atrophy or maldevelopment of the lower jaw.

Histological examination of a ranula shows that in some it is lined with columnar or cuboidal epithelium in others with fibrous tissue alone, probably as a result of destruction of the epithelial lining. In a few instances the epithelium is ciliated. The cysts are filled with clear or jelly like fluid containing mucus, but no salivary ferment.

The origin of these cysts is uncertain. They have been regarded as dilatations of the ducts of the submaxillary or sublingual salivary glands, as distension cysts of hypothetical bursæ or as retention cysts of the mucus secreting glands of the sublingual mucous membrane.

There is anatomical evidence to suggest that some of the cysts are of branchial origin and are due to prolongation forward of an unobliterated portion of the cervical sinus. It has been claimed that some of the cysts communicate with a cyst in the neck, or have a fibrous extension into the submaxillary region.

**Dermoid Cysts of the Floor of the Mouth.** A dermoid cyst of the floor of the mouth is of developmental origin and is due to inclusion of ectoderm at the time of coalescence of the two halves of the mandible. The cyst is therefore usually situated in the middle line, it lies behind the symphysis menti and between it and the hyoid bone, to either of which it may be adherent. When large, the cyst presents in the floor of the mouth and in the submental region. As growth proceeds it may deviate towards one side. When large, it may interfere with deglutition or even respiration, and the tongue may protrude.

The wall of the cyst is composed of fibrous tissue, and is lined with squamous epithelium in which sweat glands and hair follicles may be present.

**Thyroglossal Cysts in the Tongue** The suprahyoid portion of the thyroglossal duct may undergo cystic dilatation, though much less commonly than the infrahyoid portion (*see p 421*) The cyst generally appears in childhood or adolescence, and slowly increases in size It is situated in the line of the thyroglossal duct, that is, in the midline between the foramen cæcum and the mid part of the hyoid bone When the cyst arises in the upper part of the duct it projects upon the dorsal surface of the tongue in its posterior third, and in this situation it may interfere with deglutition and may even embarrass respiration When the cyst arises in the lower part of the duct above the hyoid bone it tends to project at the floor of the mouth in front of the tongue, and in this situation simulates a dermoid cyst

### TUMOURS OF THE JAWS

The jaws are subject to the same types of tumours as other bones, and they are also liable to be affected by tumours of the gums (epulis) and by tumours arising in connexion with the teeth (odontoma) There are considerable variations in the incidence of the various types in the maxilla and mandible respectively

**Tumours of the Maxilla** Carcinoma is regarded as the commonest tumour affecting the maxilla The growth may start in the mucous membrane of the nostril or of the hard palate and invade the bone secondarily, or it may arise primarily within the maxillary antrum Carcinoma of the antrum is of variable character Sometimes the cells are columnar and roughly adenomatous in formation but the cells are undifferentiated and the appearance closely resembles that of a sarcoma

Carcinoma of the maxilla is locally very malignant It invades the bone in all directions and may involve the palate, the contents of the orbit and the naso pharynx It rarely disseminates to glands or distant viscera until a late stage

Giant cell tumour of the maxilla is not uncommon It grows slowly, 'expanding' the bone, and is generally of benign character In its pathological features it resembles giant cell tumours of other bones (*see p 160*)

Sarcoma of the maxilla is now believed to be considerably less common than carcinoma It may arise near the posterior aspect of the maxilla close to the *sphenomaxillary fossa*, from the anterior aspect under the cheek, or from the region of the antrum According to its position the growth may invade the orbit and displace the eyeball, or it may project under the cheek or ulcerate into the nasal cavity Simple tumours of the maxilla are rare, apart from epulides and odontomes, which will be described separately below Fibroma, chondroma and osteoma may occur

**Tumours of the Mandible** Apart from odontomes, the commonest tumour of the mandible is a carcinoma invading the bone from the gum or the floor of the mouth

Giant cell tumour is not uncommon It occurs most often in young adults, and generally affects the body of the mandible The tumour grows slowly, and may attain considerable size It "expands"

the bone, so that the soft vascular tumour retains a thin osseous shell, and may give a characteristic crackling sensation on palpation

Sarcoma is a rare tumour in the mandible. It is generally of spindle cell type, and rapid growth

### Epulis

Epulis is a clinical term applied to outgrowths from the alveolar processes of the jaws. There are two pathological types—the fibrous and the giant-cell epulis.

The fibrous type is the more common. It arises from the edge of the gum at the neck of one of the incisor or premolar teeth. The tumour is firm, has a smooth surface, is covered by normal mucous membrane, and is often pedunculated. It grows slowly but may eventually be 3 or 4 cm. in its long axis, it may grow between the teeth and loosen them.

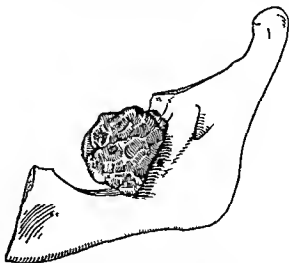


FIG 165 Epulis of giant cell type  
(Museum of Royal College of Surgeons of Edinburgh)

A fibrous epulis grows from the periosteum or from the periodontal membrane, and chronic inflammatory conditions of the gums are said to favour its development. It is a fibroma, and is composed of loosely arranged spindle cells which surround numerous blood vessels or thin walled vascular channels. Myxomatous degeneration is not uncommon. Round cells and giant cells of the foreign body type are usually present in the tumour. Certain of the growths are very vascular, and have an angioma-like appearance. They are soft and spongy, bluish red in colour, and grow more rapidly than the common fibrous type.

The giant-cell type grows more rapidly than the fibrous epulis. It is usually sessile, and forms a smooth, soft lobulated mass, covered by dark red or purple mucous membrane. It usually begins in the interior of the alveolus and as it increases in size tends to project beneath the gums; it frequently causes loosening of one or more of the teeth. In the mandible it may extend into the body of the bone, producing a cyst-like structure surrounded by a shell of bone. Microscopically, it is composed of giant cells of foreign body type in a vascular stroma of fibrous tissue.

A giant cell epulis is a benign tumour, but wide excision is required to prevent its recurrence.

### TUMOURS AND CYSTS OF DENTAL ORIGIN—ODONTOMA

An odontome is a tumour derived from the tissues—ectodermal and mesenchymal—concerned in the development of the teeth, and its pathological characters depend on the stage of development of

the embryonic dental elements when abnormal growth begins. With few exceptions the tumours are benign, but they may simulate malignant tumours.

Some of the tumours included under the heading of odontoma are not true neoplasms but are merely inflammatory overgrowths of the tissues around an unerupted tooth.

For descriptive purposes tumours associated with the teeth may be classed as follows —

A Epithelial Odontome (a) Dental cyst, (b) Multilocular cystic tumour, and (c) Dentigerous or follicular odontome

B Composite Odontome

C Connective Tissue Odontome (a) Fibrous, (b) Cementomatous

**Development of the Teeth** Knowledge of the processes involved in the development of the teeth is necessary for a correct appreciation of the mode of origin of dental tumours.

In embryos the first change which foreshadows the development of teeth is a ridge of epithelium along the line of the gum, this epithelial thickening is known as the *common dental rudiment*, and multiplication of its deeper cells at intervals causes a series of epithelial projections in the mesodermal tissues. The tip of each projection becomes cup shaped from the protrusion into it of a process of mesodermal tissue. The epithelial cup and the mesodermal projection constitute a *dental papilla* which becomes separated from the dental ridge. Normally ten dental papilla develop in each jaw to form the 'milk teeth' later however other papillae develop to form the second molars of the first dentition and three other papillae appear which represent the future permanent molars. The other permanent teeth are developed from a second series of papillae.

The cells at the summit of the mesenchymal papilla assume a columnar form and are known as odontoblasts, they give rise to dentine. The epithelial cap which covers the mesenchymal papilla becomes the enamel organ which becomes differentiated into three layers of cells—flattened stellate and columnar—from without inwards.

Each developing tooth is surrounded by a vascular fibrous tissue membrane, the *dental sac*, and the mesenchymal papilla, enamel organ, and the dental sac form together the so called *tooth follicle*.

The cement which covers the dentine of the roots of the teeth is formed from the mesenchymal tissues in the same way as membranous bone.

Tumours of dental origin may arise in the following ways (1) From proliferation of groups of cells, derived from the common dental rudiment or from the enamel organ, that may be scattered about the teeth in infancy or even in adult life. Such groups of cells were originally demonstrated by Malassez, and are known as "*débris épithéliaux paradentaires*" (2) From disorderly proliferation of the cells of a dental follicle (3) From excessive production of dental follicles.

#### Epithelial Odontome

(a) **Dental Cyst (Radiculo dental cyst)** This type of cyst occurs in adult life and usually develops in connexion with a pulpless tooth,

especially an incisor or the canines of the upper jaw. It arises from paradental epithelial rests, which are probably stimulated to proliferate by infection. The cyst is unilocular, is attached to the fang of a tooth, and is usually small, although it occasionally grows to enormous size and often extends into the maxillary air sinus and causes bulging of the cheek. A portion or the whole of the affected tooth may lie within the cavity of the cyst, but the tooth and the cyst are sometimes quite separate. Occasionally there are multiple cysts, and they may fuse (see Fig 186).

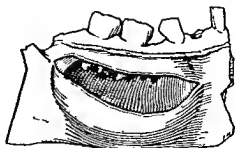


FIG 186 Large dental cyst  
(Museum of Royal College of Surgeons of Edinburgh)

A dental cyst is lined with squamous epithelium and therefore it may be mistaken for a dermoid, very rarely the epithelium is columnar, indicating more emphatically its dental origin. If infected the epithelial lining may be partly destroyed and then the walls are fibrous. The contents of the cyst are serous or mucoid and may contain cholesterol crystals.



FIG 187 Epithelial odontome. The cells of basal type lining the cysts correspond to enameloblasts. They swell become loosened towards the centre, and ultimately liquefy, thus giving rise to cyst formation.

cases tumours of this type have developed primarily in the other bones.

The tumour may be solid or cystic, it has a lobulated surface and thin walls. It causes enlargement of the alveolar border of the jaw, usually more on the outer than on the lingual aspect. From thinning of the bone, "egg shell crackling" may be detected and neighbouring teeth may be displaced. Large tumours in the upper jaw usually encroach upon the maxillary air sinus and may even extend to the

(b) Multilocular Cystic Tumour (Adamantinoma or enamel cell tumour). This tumour occurs most often in early adult life, but it has been found in childhood and in old age. The mandible is affected much more frequently than the maxilla (11/1), and the region of the angle is the usual starting point. It is usually simple and grows very slowly, and in the absence of complication such as infection, is quite painless. Very occasionally the tumour has given rise to metastases in other bones. In exceptional

orbit or to the naso pharynx. Ulceration and infection within the tumour may modify its appearance.

An enamel cell tumour has an external bony wall enclosing a solid, or more often a cystic, growth. The cysts are multiple and are filled with yellow or reddish mucoid fluid; the walls of the cysts may be smooth or lined with papillary projections. The remainder of the tumour is composed of fibrous or of bony trabeculae in varying proportions. The solid parts may resemble carcinoma, and in some specimens the connective tissue undergoes such overgrowth that it may mimic a sarcoma. Gritty particles of imperfectly formed enamel may be present.

Microscopically, the epithelial elements in these tumours are very



FIG. 138. Left half of mandible of an adult showing a follicular odontome. The un-erupted tooth is a third molar.

(Museum of Royal College of Surgeons of Edinburgh.)

variable in form, and the appearances may differ in various parts of one tumour. Three types are described which, however, have not a sharp dividing line: (1) the squamous-cell type, which shows cords of squamous cells with intercellular fibrils and cell nests, and, in addition, isolated foci of columnar enameloblasts, (2) the plexiform type, composed of convoluted columns of epithelium surrounded by a dense or cellular fibrous stroma, the epithelial cells show no tendency

to flattening, (3) the glandular type, composed of columnar enameloblasts, which may be arranged in many different ways. In all types the stroma may be dense—hyaline, myxomatous, or cellular.

This type of odontome is believed to arise from cells of the primitive enamel organ, but by some it is considered to originate from the paradental epithelial debris. It is at least certain that it is of epithelial origin.

(c) **Dentigerous Cyst (Follicular odontome, odontocoele)** This type occurs in young adults during or after the second dentition, it is more common in the lower than in the upper jaw. At the site of the cyst a tooth, usually a canine, an incisor, or a premolar, is missing. The cyst grows slowly and causes a globular enlargement of the alveolus. Adjacent teeth may be loosened and displaced. Inside the cyst there is an unerupted tooth which usually protrudes from the base of the cavity, but may be free. The wall of the cyst is usually attached at the neck of the tooth, and the root of the tooth is loosely buried in the jaw. The cement, dentine, and the root of the tooth are generally very imperfectly developed. Squamous epithelium usually lines the cyst, but occasionally cubical epithelium is present. The fluid in the cyst is glairy and contains cholesterol and broken down epithelial cells.

The origin of a dentigerous cyst is uncertain. It is generally

supposed that it arises from dilatation of the dental follicle, but as the tooth within the cyst lacks dental cuticle (Nasmyth's membrane), it has been suggested that it arises from degenerative changes in the enamel organ at an early stage of its development

### Composite Odontome

This type of tumour probably arises from disordered growth of the whole tooth germ, which results in an irregular conglomeration of dental tissues with little or no resemblance to a tooth. It occurs in subjects before the age of twenty five years and is almost always situated in the mandible. At the site of the tumour one or more teeth, especially the molars, are absent.

The tumour is hard and irregular, and lies within the jaw, it may erupt like a normal tooth and this may predispose to infection and lead to extrusion of the tumour.

Another variety of composite odontome consists of a conglomeration of imperfectly developed teeth (denticles) surrounded by a fibrous capsule lined by squamous epithelium. The teeth show variable quantities of enamel, dentine, cement, and pulp. The dividing line between this type of cyst and a dentigerous cyst is not very definite.

The mode of origin of a composite odontome is rather obscure. Some believe that it is due to misplacement of tooth follicles in early life, others that it is due to proliferation of paradental epithelium (Malassez). Ewing considered that the absence of one or more teeth in this type of tumour indicates that all the primitive dental structures—epithelial and fibrous—are concerned in the production of the tumour, and that, when there are denticles there has been over production of dental follicles. Ewing found it difficult to conceive these tumours as arising from paradental debris because of the orderly organized growth.

### Connective Tissue Odontome

*A fibrous odontome is exceedingly rare. It is overgrowth of fibrous tissue around an unerupted tooth. Rickets is believed to predispose to its development, as most examples have been found in children who have suffered from this disorder.*

Calcification and ossification may occur in the walls of a fibrous odontome giving rise to a *cementoma*.

## DISEASES OF THE SALIVARY GLANDS

### Pyogenic Infections

Acute pyogenic inflammation of the salivary glands is practically confined to the parotid and it usually terminates in suppuration—

*suppurative parotitis* The condition is most common in adults as a complication after operation but it may occur in acute febrile illnesses especially pneumonia and typhoid. It commonly occurs in debilitated persons and often heralds the fatal issue. The onset is usually sudden with painful enlargement in one parotid gland. Not infrequently both parotid glands are affected simultaneously or in succession.

*Ætiology* Dryness and uncleanness of the mouth and the diminished secretion of saliva with which these are associated are the most important predisposing factors. The dryness of the mouth is usually due to dehydration or to lack of the normal stimuli to salivation. Thus the disease very often complicates operations on the abdomen in which fluid by the mouth has been greatly restricted. Infection reaches the gland by the salivary ducts and the organisms usually present are staphylococci and pneumococci; less often streptococci and diphtheroids. The absence of mucin from the saliva of the parotid gland is believed to favour infection.

*Morbid Anatomy* The infection is multicentric and is characterized by multiple points of necrosis scattered throughout the gland, later small foci of suppuration develop and eventually may become confluent, forming an abscess which may rupture externally. The early necrosis comparable to that of a carbuncle may be attributed partly to the necrotic action of the common causative organism staphylococcus aureus and partly to the fact that the inflammatory products are confined under tension within the dense parotid fascia. The orifice of the parotid duct is swollen and red and cloudy or purulent saliva may be expressed from it. In some cases the disease is very severe and is associated with cellulitis of the neck, head and face. For a long time the pus remains confined within the capsule, later it may burst through the fascia and rupture into the external auditory meatus or point below the angle of the jaw. Untreated, the pus may burrow into the retropharyngeal space or invade the temporo-mandibular joint. Both are rare occurrences.

### Salivary Calculus—Sialolithiasis

Calculi are most common in the duct of the submaxillary gland they are much less common in the parotid duct probably because the secretion of the parotid gland is less viscid and poorer in salts.

The calculus which resembles dental tartar, is composed principally of the phosphate and carbonate of lime with a small percentage of organic matter. Probably they are formed as a result of infection, and are due to the deposition of inorganic calcium salts upon nuclei consisting of mucus degenerated epithelium and bacteria. On rare occasions a foreign body, such as a piece of straw, a fruit seed or mycelia of actinomyces may form a nucleus for stone formation.

A salivary calculus is usually single, brown or grey in colour, and slightly rough on the surface. It may be no larger than a pea, but often it is fusiform and about the size of a date stone. In the rare cases in which two or more calculi are present they may become eburrated at



their points of contact and appear to be fragments of a fractured stone

The chief effect of a salivary calculus is to cause retention of salivary secretion, and this is usually associated with periodic swelling and pain in the salivary gland, particularly at meal times, sometimes aggravated by infection. If obstruction becomes complete retention cysts may develop. As a result of continued exacerbations of inflammation the stone may lie in a bed of granulation tissue or of cicatricial tissue, and the indurated mass may be mistaken for a tumour of the floor of the mouth. In rare cases, the calculus erupts through the wall of the duct, and, in the case of the parotid, this may lead to an external fistula.

In the submaxillary gland, multiple calculi occasionally are present in the smaller ducts, and they may lead to chronic enlargement or to suppuration within the gland.

### Chronic Enlargement of the Salivary Glands

As a result of infection from the mouth sometimes following a dental extraction, one of the salivary glands may become enlarged, swollen and tender. The parotid gland is usually affected, and, at first, the inflammation is mild and subsides. Recurrence of inflammation is usual either at short or long intervals, until finally enlargement persists and other groups of glands become involved. The affected gland is the seat of chronic inflammatory changes and its duct is dilated and the seat of exfoliation. Salivary secretion is reduced its digestive properties impaired, and the infective character of the disease is borne out by the finding of leucocytes, epithelial casts and organisms in the turbid saliva from the affected gland.

**Lymphomatous Enlargement (Mikubcz Disease)** This syndrome represents the final picture of a progressive disease, the earlier phases of which may not be identified so clearly. It generally affects adult males, and leads to great disfigurement. The secretion of saliva is reduced and dryness of the mouth (xerostomia) is complained of, and conjunctivitis and pharyngitis may co exist.

The lacrimal glands are enlarged first, and only later the salivary glands. The mucous glands in the tongue and cheek may also become enlarged. The extent of the affection varies in different cases, for it may be that the lacrimal glands alone are involved or that the salivary glands are affected in various degrees. The ætiology of the glandular enlargement is unknown. No bacteria have been demonstrated, and there is no evidence that it is due to infection from the mouth or the conjunctiva.

Histological examination shows that there is a generalized lymphocytic infiltration, and there may be complete lymph follicles with germ centres. The glandular tissue is reduced in amount but shows no primary disease.

Sometimes the condition is accompanied by either local or general hyperplasia of lymphoid tissue, and sometimes there is a relative or actual increase of lymphocytes in the blood. In others, there is true leukaemia with enlargement of the spleen, etc.

**Uveo-parotitis** This is as yet an indeterminate entity, in which there is an association of inflammatory lesions of the ocular tract and of the parotid and sometimes other salivary glands

The enlargement of the parotid gland appears abruptly and may be attended by fever, it is either preceded or followed by irido-cyclitis. In a large proportion of the cases unilateral or bilateral facial paralysis develops and persists for a variable time. There may be temporary paralysis of other nerves. In many cases skin eruptions of a tuberculate type are present.

The swelling of the affected salivary gland is firm, nodular and painless. It is the seat of fibrous tissue proliferation and microscopically in most cases there is separation of the glandular acini as a result of infiltration by lymphocytes and giant-cell aggregations resembling tubercles.

The ætiology of uveo-parotitis is obscure. There is good evidence to suggest it is like Mikulicz disease a manifestation of sarcoidosis.

The disease occurs most often in women especially in the second and third decades. It pursues a chronic course lasting for weeks or months. Recovery is generally complete, but there may be relapses. There may be residual ocular defects as a result of synechia and keratitis.

fibrous capsule. The cells show various forms—spheroidal, cuboidal, spindle, or even squamous, with a small, darkly staining, angular nucleus. When myxomatous tissue is present it lies in juxtaposition to the cellular components, from which it is probably derived. More detailed examination shows that in many parts of the tumour the cells are arranged in irregular masses or branching columns; but usually there are vague or definite duct or alveolar formations suggesting a reproduction of the normal gland structure. Thus, taking into account the common variations from the standard pattern, there are types which may be regarded as an adenoma, types, more cellular and with less differentiation, which might be classified as either adeno-carcinoma or sarcoma. Mitosis and irregular proliferation (rather than the cellularity of the tumour) form the most reliable criterion of malignancy.

The origin of salivary gland tumours is an academic problem. Their common epithelial ancestry is suggested by the gradations in differentiation in various examples; in one there may be little but myxomatous tissue, in another well-formed tubule formations, and in many merely suggestions of genuine epithelial origin.

A recurring controversy is that of the origin of myxomatous (or mucoid) tissue within the tumours. It has the appearance of cartilage in stained secretions, but more specific stains suggest it is due to degeneration or is a derivative of the cellular components (or possibly the stroma), rather than an accidental inclusion such as would suggest a branchio-genetic sequestration in the territory of the salivary glands. Such mucoid tissue is not uncommon in other tumours, e.g., sebaceous adenoma and tumours of the testis, and can be interpreted, as in these examples, as a cellular by-product rather than an independent tissue formation.

#### Adenolymphoma of the Salivary Glands

This rare tumour occurs in late adult life, especially in the parotid gland in the preauricular region or at the angle of the mandible. It is a



FIG. 189. Mixed tumour of the parotid gland. The cells are arranged irregularly, but in places there is evidence of tubule formation. A large amount of mucoid tissue lies between the masses of epithelial cells.

(Laboratory of Royal College of Physicians of Edinburgh.)

simple readily enucleable tumour seldom reaching a size greater than a walnut. It may be solid but is more often cystic and contains mucoid or turbid fluid. Microscopically it consists of columnar epithelium supported by a lymphoid stroma with active germ centres. The solid portions of the tumour may be composed of gland acini.

It is believed that the tumour is derived from ectopic salivary gland epithelium within lymphoid tissue, although a branchial origin cannot be excluded.

### BRANCHIAL CYSTS AND FISTULÆ

A branchial cyst is of developmental origin and takes origin from remnants of the cervical sinus—the ectoderm lined space, formed by the second branchial arch as it overgrows the more caudal arches.

A branchial cyst forms a rounded tense swelling below and behind the



FIG 190 Branchial cyst

angle of the jaw, it usually occurs in early adult life and is often mistaken for a tuberculous gland (*see* Fig 190). The cyst has fibrous walls and is seldom larger than a golf ball, it lies deep to the cervical fascia and is partly covered by the sternomastoid muscle. It is in contact with the carotid sheath and a prolongation of the cyst may bulge between the carotid vessels. The lining membrane of a branchial cyst is squamous epithelium which generally shows keratinization, a variable amount of lymphoid tissue is usually present in and around the cyst

wall. The contents consist of glairy mucoid fluid which generally holds in suspension a large number of cholesterol crystals and desquamated epithelium. The discovery of cholesterol crystals on aspiration is a valuable diagnostic sign.

The cyst may be the seat of recurrent attacks of inflammation, and in rare instances suppuration occurs. A persistent sinus may result from incision of the cyst. It is doubtful if a carcinomatous change ever occurs in the lining epithelium.

In rare instances a small deeply seated cyst is found at autopsy attached to the external surface of the pharynx. This variety of cyst is

lined by columnar epithelium, which may be ciliated. It rarely gives rise to signs or symptoms unless infected, it is believed to originate from the mucous membrane of one of the primitive pharyngeal clefts.

A *branchial fistula* or *lateral fistula of the neck* is a blind track which extends upwards from the skin surface of the neck deeply towards the pharynx. The orifice of the sinus is usually situated at the anterior border of the sterno mastoid muscle about 4 to 6 cm. above the sterno clavicular joint. The sinus may remain permanently open and discharge a little serous fluid, or it may be closed for long periods.

The fistulous tract forms a cord like structure with a small, slightly tortuous, irregular lumen. It is lined with several layers of columnar epithelium which is generally ciliated, but sometimes shows squamous metaplasia. A large amount of lymphoid tissue is present in its walls. When traced upwards the fistula is found to sink gradually through the superficial fascia and the platysma, and at the upper border of the thyroid cartilage it pierces the deep fascia. In its further course it lies superficial to the internal carotid artery and the glossopharyngeal nerve, but deep to the lingual, occipital, and external carotid arteries. It is crossed by the hypoglossal nerve and the stylomandibular ligament. The fistulous tract ends in the region of the supratonsillar fossa. It is believed that originally a membrane separated the fistula from the pharynx. In cases seen surgically, however, the fistula may communicate with the pharynx.

A branchial fistula is generally regarded as due to persistence of the *cervical sinus*, the ectoderm lined track corresponding to the second branchial cleft. This view fails to account for the character of the lining membrane of the fistula, which is usually of ciliated columnar character. An alternative theory, which seems more plausible, attributes the fistula to persistence of the thymopharyngeal duct.

*Branchiogenetic carcinoma* has been described. The tumour is a squamous cell carcinoma of horny type, very hard and indurated, and sometimes partly cystic. It arises deeply in the neck, in close relation to the carotid vessels, and infiltrates widely at an early stage. The microscopic appearance of such tumours is very diverse and the cells may resemble those of a carcinoma or of a sarcoma, most often they are "prickle cell" type. A feature which is generally held to signify the branchiogenetic origin of the tumour is the layer of lymphocytic tissue which encapsules the tumour. Nodules of cartilage may occur in the tumour.

While this is the description applied to branchiogenetic carcinoma, it must be emphasized that the branchial origin of such tumours is difficult of proof. In some cases, doubtless, tumours of this character are actually secondary growths, from a primary focus in the nose, pharynx, Eustachian tube, larynx, accessory air sinuses or thyroid gland.

## TUMOURS OF THE CAROTID BODY (Paraganglioma Perithelioma)

The carotid body is situated at or about the bifurcation. It is developed from embryonic ganglion cells of the sympathetic nervous

system. Normally, it is composed of polyhedral cells collected into spherical clumps or nodules. Some of the cells stain dark brown with chromic acid (chromophil), like those of the suprarenal medulla, but they do not contain adrenalin. The gland normally contains a few nerve ganglia and non medullated nerve fibres. It is very vascular and is supplied by a special arteriole and venule.

Tumours of the carotid body are rare. They appear most often about puberty and give rise to a protruding swelling in the neck.

The tumour may attain the size of a hen's egg. It may be firm or soft, and is sometimes pulsatile, and in many cases the surface is covered by numerous large, tortuous vessels. A definite capsule is usually present, from which septa pass to the inside of the tumour. The cut surface has a spongy, pink or greyish red appearance, and there is often evidence of hæmorrhage. From their shape, lobulation and greyish surface such tumours have been called "potato tumours".

The growth applies itself closely to the carotid vessels, which often become incorporated in the tumour or may even be compressed by it. Owing to its fixation to the vessels the tumour is movable laterally but not vertically.

Microscopically, the tumour shows very variable features and it has therefore been found difficult to devise a satisfactory pathological designation for it. The common appearance, in the more differentiated parts of the tumour, is that of masses of polyhedral



FIG 191 Carotid body tumour. The cells are large and clear and are in solid alveoli.

(Laboratory of Royal College of Physicians of Edinburgh.)

granular cells arranged in whorls around blood vessels, and nerve twigs are often incorporated within the cell bundles. Chromaffin may be evident in the cells. The blood vessels, in the form of sinusoids, may be very numerous and give the tumour a hæmangiomatous appearance. There is evidence, on histological grounds, that the tumour is akin to the glomus tumour of the skin and the neuroblastomas of the sympathetic nervous system.

The majority of carotid body tumours are innocent and grow very slowly. But in a few instances, after persisting for many years they may suddenly show rapid growth with features of malignancy, evidenced by local infiltration. Metastases may arise in the lymph glands but distant metastases do not occur.

From the surgical point of view it is found that the tumour may be shelled out in a few cases. But in others, on account of adhesion to the carotid artery, jugular vein, and large nerves, it may be necessary to sacrifice parts of these structures. It is for this reason that the operative treatment of carotid body tumours is often a serious undertaking. The mortality rate is about 30%, and this is accounted for by cerebral oedema, following on ligation of the carotid vessels.

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## CHAPTER XX

### DISEASES OF THE THYROID GLAND

#### ANATOMY AND PHYSIOLOGY

THE normal thyroid gland is pale pink in colour, of soft consistency, and smooth or slightly uneven on the surface, it is enclosed in the pretracheal layer of the cervical fascia. The cut surface is greyish red and glistens lightly from the colloid it contains.

The gland is divided into lobules by connective-tissue stroma derived from intrusions of its areolar capsule. Each lobule contains a number of acini or cubical follicles. The acini vary in diameter and are spherical or polyhedral and lined with a single layer of epithelium. The cells have no basement membrane and rest directly on a stratum of areolar tissue in which lie numerous blood and lymph channels, the finer vessels are sinusoidal and lie in contact with the vesicular epithelium. Adjacent to some of the acini there are groups of spheroidal cells whose function is probably to replace effete vesicles. Lymphocytes are present in the interstices of the gland and aggregations of them may be a prominent feature.

The acini are filled with an iodine-containing viscous fluid—*colloid*—which stains bright pink with eosin. The colloid containing droplets of the specific hormone is the product of the thyroid cells, and the amount in the vesicles varies inversely with the activity of the gland. Generally it may be assumed that an excessive accumulation denotes inactivity on the part of the gland (*storage phase*) and diminution signifies activity of the gland (*secretory phase*).

The appearance of the vesicles varies with the state of activity of the thyroid. The resting vesicle is distended with colloid, the cells are cubical, the protoplasm of the cells and of the centrally placed nucleus stains rather faintly and shows few granules. The active vesicle is irregular in shape and is collapsed, colloid is absent or present only in small amount and is more fluid, the cells are larger and tend to be columnar, their nuclei are larger and placed peripherally, and the granules stain more deeply.

The thyroid gland has the special property of abstracting iodine from the blood. Normally the iodine content amounts to 0.01 to 1.15% of the dried weight of the gland—amounts in striking contrast to 0.001%, the maximum for any other tissue. The avidity of the gland for iodine is illustrated by the experiments of Marine and Rogoff, who showed that in dogs intravenous injection of 50 mgm. of potassium iodide increased the iodine content by several hundred per cent. in five minutes. The iodine content of the blood varies in different localities and in diseases of the thyroid gland. The average level is 6 to 8 gamma per cent., but in subjects of hyperthyroidism it may exceed 50 gamma per cent. Iodine in the blood occurs in an organic and an



inorganic fraction and the relative amounts of each vary, and estimation of their relative proportions may be of value in the study of thyroid function and disease.

Iodine is utilized by the thyroid gland in the elaboration of its specific hormone—*thyroxin*. Thyroxin was first isolated from the gland by Kendall in 1915 and was prepared synthetically by Harrington in 1927. The biological effects of thyroxin are obvious in human beings after the administration of thyroid extract. It gives rise to tachycardia, flushing of the skin and an increased metabolic rate, but the most conspicuous signs of pathological thyrotoxicosis *viz*, exophthalmos, tremor and dilatation of the pupil do not occur. But, recently it has been shown that if thyroid extract is given with drugs such as ephedrine, which stimulates the sympathetic nervous system, exophthalmos develops.

There is a close relationship between the thyroid and the anterior lobe of the pituitary gland. Removal of the anterior lobe of the pituitary is followed by partial atrophy of the thyroid, and, conversely, prolonged administration of pituitary extracts leads to hyperplasia of the thyroid. Thyroidectomy is followed by hypertrophy of the anterior lobe of the pituitary.

It is now known that the anterior lobe of the pituitary contains a specific thyroid stimulating hormone, which, even *in vitro*, affects its cells. Confirmation of the stimulatory action of the pituitary is evidenced by animal experiment (*e.g.*, in ducks) in which continued injections of extracts produce massive hypertrophy of the thyroid accompanied by exophthalmos.

## CLASSIFICATION OF DISEASES OF THE THYROID GLAND

The conceptions of the pathology have been greatly simplified since the importance of iodine deficiency as a causative factor in simple goitre has been recognized and since the essential unity of the toxic forms has been appreciated. It is usually difficult to correlate the functional disturbance of thyroid disorders with structural abnormality of the gland.

The various clinical conditions can be considered conveniently under the following headings: (1) congenital abnormalities, (2) acute and chronic thyroiditis including lymphadenoid goitre (*struma lymphomatosa*) and ligneous thyroiditis (*Riedel's struma*), (3) Simple goitre, (*a*) parenchymatous, (*b*) diffuse colloid, (*c*) adenomatous, (4) goitre with thyrotoxicosis (*toxic goitre*), (*a*) primary (*exophthalmic goitre*), (*b*) secondary (*toxic adenoma*), (5) tumours.

## CONGENITAL ABNORMALITIES

The thyroid gland is developed as early as the third week (1.5 mm embryo) as a median outgrowth of the endodermal lining of the floor of the pharynx. The bud as it elongates becomes hollow and its end globular. Evidence of a bilobed structure can be found in a 5 mm

embryo. The connexion of the stalk (now solid) with the pharynx is lost in the 7 mm embryo and the separation may occur near the pharynx or more caudally. Separation near the pharynx is believed to favour persistence of a pyramidal lobe or a thyroglossal duct, whereas detachment at a lower level may account for a lingual thyroid rest or a suprahyoid cyst.

Descent of the thyroid gland is probably determined by the caudad movement of the primitive heart and its aortae and abnormal evolutions of these structures may lead to ectopia of the thyroid or aberrant glands.

A lingual thyroid may be associated with absence of the thyroid gland in the neck or it may be a supernumerary gland. It is situated in the median raphe beneath the mucous membrane at the base of the tongue. It is yellowish red like a cherry, and is generally sessile, but is occasionally pedunculated. Large and dilated vessels may traverse its surface.

The swelling at the back of the tongue may attract attention in childhood on account of dysphagia or respiratory obstruction, but more often is unnoticed until puberty or pregnancy, when, from increased vascularity, hæmorrhage, or degeneration, it increases in size. Rarely, malignant change occurs.

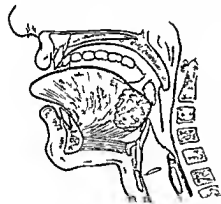


FIG 192. Diagram of lingual thyroid  
(Department of Surgery University of Edinburgh)

**Aberrant and Accessory Thyroids.** Nodules of thyroid tissue, single or multiple, and of varying size, may occur in the line of the pyramidal process. They may constitute the entire thyroid or be supernumerary glands. Similar nodules may be present in proximity to the inferior extremity of the gland or, in rare instances, in the mediastinum, or even embedded in the larynx or trachea where it may cause suppuration.

More commonly outlying and separate nodules of thyroid tissue

occur in the anterior or posterior triangles of the neck on one or on both sides. They may undergo enlargement either alone or in conjunction with the normally placed thyroid. The origin of such laterally placed portions of thyroid is believed to be from the ultimobranchial body, and it is conceded that they are specially prone to malignancy, resulting in a papilliferous type of carcinoma. Their dark colour may suggest a melanotic tumour. There is evidence that some such outlying nodules are not of developmental origin but are the result of metastasis to glands from an inconspicuous papilliferous carcinoma of the thyroid on the same side. Supporting evidence is the constancy of the lymphoid capsule the tumours retain and the occasional presence of papilliferous changes within the thyroid gland.

**Thyroglossal Cysts and Fistulae.** A cyst may occur at any point in the course of the thyroglossal tract, from the foramen caecum to

the isthmus of the thyroid gland, or even as low down as the supra-sternal notch. Very occasionally the cysts are multiple. Remnants of the thyroglossal tract are rare above the hyoid, and therefore cysts are correspondingly uncommon in that situation, but, below the hyoid bone, remnants of the tract are often present and cyst formation is consequently fairly common. When the infrahyoid part of the tract is complete it extends in the middle line or slightly to one side of it from the isthmus of the thyroid gland to the hyoid bone, behind which it is usually enfolded.

A thyroglossal cyst may be present at birth, but in the majority of cases it first appears in childhood or in early adult life. The cyst, which varies in size from a pea to a walnut, forms a rounded, tense swelling in or close to the middle line of the neck. Most commonly it lies immediately below the hyoid bone but it may be as low as the cricoid cartilage or even the supra-sternal notch. Much more rarely the cyst is situated above the hyoid bone and, in that situation it may bulge into the substance of the tongue or even into the floor of the mouth as well as beneath the chin. The cyst is thin walled and contains clear, glairy or mucoid fluid, occasionally the contents are dark from cholesterol crystals or altered blood. The cyst is lined with stratified columnar, cubical, or squamous epithelium in varying proportions. Small islets of thyroid tissue may be present in the wall of the cyst. In many cases a considerable amount of lymphoid tissue surrounds the cyst and pre-disposes it to infection. Frequently a narrow fibrous band extends from the wall of the cyst to the posterior and inferior part of the body of the hyoid bone, and sometimes this prolongation may actually traverse the bone, or it may pass in front of the hyoid and extend to the base of the tongue.



FIG 193 Thyroglossal cyst

A thyroglossal cyst is very liable to infection especially after an attack of pharyngitis and if suppuration occurs the cyst may rupture and form a fistulous opening in the neck—*thyroglossal fistula* or *median fistula of the neck*. In other instances a fistula results from aspiration or from incomplete removal of the cyst. The fistula is very persistent and discharges glairy fluid or pus continuously or intermittently. Usually a firm cord of tissue can be felt passing from the fistula towards the hyoid bone, and as a result of fibrosis and contracture of the cord, the skin surrounding the orifice is indrawn and forms a crescentic fold.

Surgically, thyroglossal cysts and fistulæ, on account of their ramifications, require specially planned operations for their eradication. As the prolongation of the cyst or fistula is often attached to the hyoid bone or extends towards the base of the tongue, it is usually necessary to remove a portion of the bone and to excise a tubular portion of the median fibrous raphe of the genio-hyoid muscles.

### ACUTE THYROIDITIS

Acute thyroiditis is rare in healthy thyroid glands, but is not uncommon in goitrous ones. It may occur as a complication of various infective diseases especially those of the respiratory tract. One or both lobes of the gland may be affected. The inflammatory process usually subsides, but suppuration may occur and the resulting abscess may burrow into the œsophagus, the trachea, or the mediastinum.

In rare instances suppuration follows perforation of the œsophagus or the trachea by a sharp foreign body. Carcinoma of the pharynx or of the œsophagus may invade the thyroid gland and lead to suppuration.

### CHRONIC THYROIDITIS

**Tuberculous Thyroiditis.** Tuberculosis of the thyroid gland is very rare. It is secondary to tuberculosis elsewhere, and it may affect a healthy gland or an adenomatous one. It may occur in one of three forms: (1) *miliary*, which is similar to miliary tuberculosis of other organs, (2) *caseous*, an uncommon form, sometimes associated with tuberculous lymphadenitis, and (3) *sclerosing*, in which one lobe or the entire gland is the seat of extensive fibrosis, and is hard, elastic, yellowish white, and fixed to surrounding structures.

**Syphilitic Thyroiditis.** Syphilis of the thyroid is rare. It may occur in inherited syphilis and it develops usually in early adult life. It may occur also in acquired syphilis.

In syphilitic thyroiditis the gland is moderately enlarged and is diffusely infiltrated by fibrous tissue. It is usually slightly nodular and extremely hard, and as the thyroid often adheres to surrounding structures, resemblance to malignant disease may be very close. In many cases symptoms referable to pressure on the trachea are present and may become urgent.

### Lymphadenoid Goitre: Struma Lymphomatosa (Hashimoto's disease)

This non specific form of goitre was first described in 1912 by Hashimoto. It possesses characteristic pathological features which class it as a distinct form of thyroid abnormality.

It occurs almost exclusively in females at ages ranging from adolescence to late life, and frequently culminates in myxœdema, though in rare instances toxic features may appear. The thyroid gland is moderately and uniformly enlarged, smooth and firm, and when cut is pale pink or yellow in colour. Everywhere there is an increase of fibrous tissue leading to exaggeration of the normal lobulation. Colloid containing tissue is absent. Microscopically, the characteristic feature is

the uniform and widespread infiltration with lymphocytes, together with many germ follicles, which replace, distort, and lead to acinar degeneration. In the later stages there may be extensive fibrosis.

The pathogenesis of this variety of goitre is obscure. McCarrison reproduced a similar type in rats fed on a deficiency diet. However, in man there is little evidence that dietary deficiencies are responsible.

Attempts have been made to establish a relationship between lymphadenoid goitre and ligneous thyroiditis, and there are now records of so many examples in which the pathological characteristics appear to be so blended that the unity of the two conditions is likely to be substantiated.

### Ligneous Thyroiditis (Woody Thyroiditis; Riedel's struma)

This rare form of thyroid affection was first described in 1896 by Riedel, who summed up its main features as "a chronic inflammation of the gland leading to the formation of an iron hard tumour." The disease is of importance because of its simulation of carcinoma, and its possible relationship to lymphadenoid thyroiditis.

The most conspicuous feature is a painless enlargement of the thyroid, which is densely hard. The gland is adherent to the trachea and other structures of the neck, and pressure symptoms are generally severe and are out of proportion to the degree of enlargement. Women are more often affected than men, and usually the disease is not associated with either hypothyroidism or hyperthyroidism. The regional lymph glands are not enlarged. Spontaneous retrogression of the disease has been reported, and retrogression has also been known to occur after removal of part of the gland or after exposure to radium.

**Pathology.** The appearance of the thyroid gland and its relationship to surrounding structures varies according to the duration of the disease. In the

early stage it is enlarged irregularly and asymmetrically. Its surface may be smooth or nodular, and the gland is extremely hard, so that a sensation of iron hardness is imparted when an attempt is made to cut it. The cut surface may show thick grey hyaline bands of fibrous tissue which intersect the gland. The gland is usually adherent to its fascial capsule, and, at a later stage, may be tightly bound to the muscles, trachea, and the carotid sheaths. In the advanced stages, tough, leathery



FIG 191. Ligneous thyroiditis  $\times 55$ .  
The gland is extensively infiltrated with fibrous tissue containing many lymphocytes.

(Department of Pathology, University of Glasgow.)

the soil or in foodstuff borne by it. Probably in many instances intake of iodine is adequate, but its utilization is disturbed by alimentary or constitutional abnormalities. However important iodine deprivation may seem in goitre areas there is not sufficient evidence to prove that it bears an inverse ratio to the incidence of the disease. It is more likely that deficiency of iodine renders the metabolic processes more susceptible to the action of additional goitrogenic agents. In brief, iodine may determine endemism, superimposed factors (so called goitrogenic agents) its incidence.

*Goitrogenic agents* include (1) insanitary conditions, (2) faulty diet, (3) chemical substances.

(1) *Insanitary conditions* which permit of contamination of food and drinking water by human and animal excreta have been proved to be fruitful predisposing causes of goitre in localities where the iodine content in the soil is low and the diet faulty. Provision of a purified water supply brings about a notable reduction in the incidence of goitre in such regions.

(2) *Faulty diet* may give rise to goitre in animals under experimental conditions and presumably may have the same effect in man. The most important agencies are (a) excess of fats, fatty acids and lime, (b) deficiency of iodine, vitamin A, vitamin C, and protein (in association with vitamin A deficiency) (c) the presence in the diet of certain substances such as cyanogen compounds found in cabbages. The iodine content of fresh foodstuffs varies greatly in different localities. The minimum requirement of iodine for adults is said to be about 15 mg per day, but lesser amounts may be adequate provided positive goitrogenic agents are eliminated.

(3) *Chemical substances* have been shown to be goitrogenic in animals. The best known are calcium, boron, silica, organic acids and cyanides. Cyanides apparently act by depressing tissue oxidation, with consequent greater thyroxine requirement and an increased iodine supply to meet its production.

**Prophylaxis of Goitre.** Striking evidence of the importance

of iodine in the prevention of goitre is afforded by statistics from goitre regions following upon the practice of supplying tablets containing



FIG 193 Photomicrograph of colloid goitre. Note the enlargement of the acini due to excessive accumulation of colloid and the flattening of their epithelial lining.

10% to 15% of thyroid glands examined at autopsy display either macroscopic or microscopic evidence of adenomatous changes

Formerly the nodular masses characteristic of this type of goitre were regarded as innocent tumours, but they are now believed to represent circumscribed areas of involution developed in a hyperplastic gland. They have their counterpart in chronic lobular mastitis and in some types of cirrhosis of the liver.

The mode of origin of the adenomatous masses is probably as follows. In the process of involution subsequent to hyperplasia the restoration to normal is not necessarily uniform, some parts may remain in a state of hyperplasia, others may involute completely, and others may undergo excessive involution. When the involutionary changes are confined to individual lobules and the rest of the gland remains either temporarily or permanently in a state of hyperplasia the colloid filled vesicles of the involuted portions of gland become demarcated from the rest and this segregation may become more pronounced by the condensation and overgrowth of fibrous septa which afford an adventitious capsule for the nodules. In a somewhat similar manner persisting areas of hyperplasia may become delineated from the rest of the gland resulting in a more solid type of adenoma. Such a cycle of changes in the thyroid gland may be evolved rapidly or may occupy many years, and as an outcome, the histological appearances may be very complicated. For example, in one gland there may be areas typical of colloid goitre, of adenomatous goitre, and of all grades of hyperplasia.

#### Morbid Anatomy

The appearances of the thyroid are extremely varied. Sometimes there is a single adenoma, but more often the tumours are numerous and scattered throughout one or both lobes, and, as a result, the gland may be greatly enlarged. An individual adenoma may be no larger than a pea or it may be as large as an orange. It has usually a well formed capsule, and if single it can be enucleated. On section it may have a gelatinous or amber appearance, or it may be firm, greyish yellow and elastic.



FIG 19— Adenoma of thyroid gland the tumour has been bisected  
(Department of Surgery University of Edinburgh)

A thyroid adenoma of whatever type is very liable to complications. A solid adenoma may undergo necrosis, a colloid adenoma frequently becomes cystic. The cyst contents are often chocolate coloured from extravasated blood, and cholesterol crystals may be present. Haemorrhage into an adenoma is a fairly frequent occurrence, it may lead to sudden enlargement of the adenoma and may therefore simulate

acute thyroiditis or even malignant disease. Calcification may occur in the capsule or septa of an adenoma or within its partly necrotic contents.

Microscopically, it is customary to distinguish two types of adenoma, the *colloid* and the *follicular*. The colloid type is composed of large colloid-filled acini, occasionally interspersed with nests of hyperplasia. The capsule is usually well formed and the surrounding acini are compressed. The remainder of the gland may be normal or it may show diffuse or patchy hyperplasia. In the follicular type, which is



Fig. 194. Adenoma of thyroid gland.  $\times 75$ .  
(Department of Pathology, University of Glasgow.)

usually single, the acinar structure is seldom obvious, the cells are usually cuboidal or spheroidal with large dark staining nuclei and are arranged compactly or in strands or columns, sometimes interspersed with hyaline stroma. Colloid is seldom present in large quantity.

### TOXIC GOITRE OR HYPERTHYROIDISM

During recent years there has been a tendency to unification in the classification of the various types of toxic goitre, and for descriptive purposes it is convenient to divide cases into two fairly well-defined groups: (1) primary (exophthalmic goitre, primary Graves' disease), and (2) secondary (toxic adenoma).

The term *primary toxic goitre* signifies that toxic features have developed while the thyroid gland is healthy and capable of very prolific activity, whereas the designation *secondary toxic goitre* is applied to those cases in which toxic features develop in connexion with a gland whose activity is altered by disease, either hyperplasia, colloid, or adenomatous goitre. It should be borne in mind that the difference



between the two types is one of degree rather than of kind and that all gradations between them may be recognized. In short toxic goitre (which includes both forms) is a single disease, and its manifestations in different cases are merely modified according to the condition of the thyroid gland when the particular stimuli to activity are imposed upon it, and to a less extent according to the age and the constitution of the patient. In Britain the sex incidence of thyrotoxicosis is about eight females to one male.

**Ætiology.** All are agreed that the features of toxic goitre are due only to excessive output of thyroxin by the thyroid gland. On an average the blood level is from 8 mg. to 14 mg. compared with 4 to 5 mg. in normal persons and very constantly the organic fraction of blood iodine is increased. There is no proof that the excessive secretion is of a different character from the normal. Many attempts have been made to incriminate other endocrine glands in the initiation of the disease and in the final manifestations in various systems of the body. An excessive output of thyrotropic hormone from the pituitary gland has been held responsible but the evidence is not yet complete.

The predisposing causes of toxic goitre are fairly well known. *Primary toxic goitre* occurs most often in young subjects especially women and may sometimes develop before puberty. Not infrequently there is history of goitre in the family. Less often the disease develops about the time of the menopause.

The exciting causes of toxic goitre are suggested by the frequency with which a history of nervous strain precedes the illness. It may be acute or protracted and subjects of an emotional or artistic temperament are more susceptible. In other instances infections such as



FIG. 199. Primary toxic goitre associated with hypertrophy of thymus gland.  
(Department of Surgery University of Edinburgh)

*Secondary toxic goitre* usually develops in older subjects usually women after thirty five years of age or much later.

influenza tonsillitis etc precede the illness and may be regarded as exciting factors

### The Thyroid in Toxic Goitre

(a) **Primary Toxic Goitre** The thyroid gland is enlarged uniformly to a moderate degree. On an average it is about four or five times the normal size, but in some cases the enlargement may not be obvious on examination as the gland sometimes insinuates itself behind the trachea. There is no constant relationship between the size of the gland and the severity of the symptoms. The gland is highly vascular owing to dilatation and proliferation of its blood vessels. The cut surface is granular and friable and owing to the diminution of colloid it lacks the normal glistening appearance. In old standing cases there may be a marked increase of the intraglandular stroma. The iodine content of the gland is reduced. In the majority of cases of toxic goitre beginning before the age of thirty years the thymus shows hyperplasia. In some cases

the lymphoid tissue throughout the body shows a mild degree of hyperplasia.

Microscopically, the most characteristic features are reduction in the amount of colloid and proliferation of the epithelial cells lining the acini. The colloid is usually very scanty and is more fluid than normally and is often vacuolated; it often contains degenerated cells and it stains poorly with eosin. The cells of the acini are enlarged and swollen, increased in number and definitely columnar. Infolding of the walls of the acini



FIG. 200. Photomicrograph of thyroid gland from a case of primary toxic goitre. The epithelium of the acini shows marked hyperplasia; the colloid is scanty and vacuolated.

is usually a striking feature and as a result the acini lose their normal shape. An excess of lymphocytes is present in many cases.

The appearance of the thyroid gland in primary toxic goitre varies according to the clinical course of the disease. In cases which run a rapid course without remissions there are only the changes of hypertrophy and hyperplasia as described above, whereas in cases in which there are natural remissions parts of the gland are hyperplastic and others involuted. In the involuted parts the acini are distended with colloid, and as the involutionary process usually has a lobular distri-

bution these colloid areas frequently become separated from the rest of the gland, forming adenomatous or nodular masses of varying size. The areas of hyperplasia also have a lobular distribution and may become sharply demarcated to form the so called "miliary adenomata."

Similar involutionary changes follow the therapeutic administration of iodine in primary toxic goitre. They include restoration of colloid to the vesicles, disappearance, in places, of hyperplasia and hypertrophy, and increase of the fibrous stroma and reduction of vascularity. As a result the gland becomes firmer and more gelatinous, and often distinctly mammillated or nodular on the surface. It is well known that iodine produces very marked temporary amelioration and reduction of basal metabolism in over 70% of cases and rarely fails to effect some benefit.

(b) Secondary Toxic Goitre (Toxic Adenoma). In most cases the pre-existing pathological condition is an adenomatous goitre, which may have been present since early adult life. The adenoma, *per se*, does not confer any special tendency to the development of toxicity, but it alters the toxic features very considerably. It appears as if the epithelium in an adenomatous goitre is already, to some extent, exhausted or destroyed, and is unable to react to the same extent as a healthy gland, and therefore the manifestations of secondary toxic goitre are usually less pronounced than those of the primary variety, though the effects upon an already impaired cardiovascular system may be more grave.

It is presumed that excessive secretion is not elaborated in the adenomata but in other parts of the gland, but in a very few cases it must be conceded that a single adenoma, situated in an apparently healthy gland, may be itself responsible for toxic effects, for removal of the adenoma (which is often of small size) rapidly brings about relief of the hyperthyroidism.

**Hyperthyroidism and Thiouracil Drugs.** The discovery of potent antithyroid drugs (thiouracil, etc.), has simplified the control of hyperthyroidism. The agents have no effect upon the cellular or vascular elements of the gland which are totally unaltered after prolonged dosage. Their mode of action, so far as is understood, is by inhibition of the normal synthesis of thyroxin, and it has been suggested that the drug deters the enzyme process (peroxidase) present in the synthesis of thyroxin. The suppressive effects of the agents is gradual and progressive, and a drop of about one degree of metabolism per day is usual. On an average if there is no intolerance, the constitutional effects of hyperthyroidism are under control within 4 to 7 weeks. The thyroid gland remains hyperplastic, but is still susceptible to the involutionary changes which iodine confers. Thus, in practice, it is usual, when thyroidectomy is contemplated, to administer iodine for some 10 days after the full effects of the antithyroid drug have been received.

**Exophthalmos.** Exophthalmos is one of the most arresting features of toxic goitre. It is probably due to a combination of causes chief of which are (a) sustained contraction of unstriated muscle fibres within the orbit and eyelids, (b) increase of fat in the socket of the eyeball, and (c) adenomatous infiltration of the ocular muscles.

Protrusion of the eyes usually diminishes after surgical treatment of the goitre, but in a few instances (especially in elderly males) it persists or increases, so much so that the eyelids cannot be closed and the cornea is permanently exposed and becomes ulcerated. Continued infection may lead to destruction of the eye (exophthalmic ophthalmoplegia). The persisting exophthalmos is believed, as in experimental conditions, to result from excessive liberation of the pituitary factor responsible for thyrotoxicosis. It may retrogress when the whole thyroid is removed.

## TUMOURS OF THE THYROID GLAND

### Adenoma

In a previous section it was indicated that the common nodular formations in the thyroid are not true tumours. But there is a small group which have undoubted features of an adenoma. Such a tumour, often called "foetal adenoma" from the primitive character of its cells, is usually single, small, solid, and well encapsuled. Histologically, it is composed of cubical or spheroidal cells containing large dark staining nuclei and very little faintly staining protoplasm. In the early stages the cells lie in sheets without a lumen or are arranged in columns. In places a lumen may form and a minute amount of colloid appears and the tumour then has the appearance of the thyroid gland in infancy. Development may proceed and large vesicles filled with colloid appear, but the cells lining them remain small and other parts of the tumour retain their undifferentiated character. The remainder of the gland is usually healthy. The tumour is generally functionless, and is prone to early degeneration leading to cyst formation. In rare instances myxœdema has followed removal of a thyroid adenoma, even though the gland appears healthy.

### Carcinoma

Carcinoma of the thyroid usually occurs between the ages of fifty and seventy. Unlike other thyroid diseases the incidence is relatively greater in men than women (2.4:1).

Carcinoma is specially prone to develop in a gland already altered by disease, particularly the adenomatous type of goitre. For this reason the incidence of malignant disease of the thyroid is high in endemic goitre regions.

Usually malignant disease of the thyroid gland causes neither hyperthyroidism nor hypothyroidism, occasionally, however, the tumour or its metastases elaborate thyrotoxin and thus lead to the changes characteristic of toxic goitre.

The histological appearance in carcinoma of the thyroid gland is very diverse, varying from an epithelial proliferation not dissimilar to that of toxic goitre to a degree of anaplasia which may lead to confusion with sarcoma. It is customary, however, to recognize the following pathological types of growth, although it should be understood that they are not invariably distinct and that many intermediate forms

occur. Of these types, the first three are not uncommon, the others rare

**Malignant Adenoma** This tumour occurs especially in endemic goitre regions. It is thought to arise most often in a foetal adeoma. The tumour varies considerably in size and appearance. It may attain large size and exercise its malignant effects mainly by pressure in the neck, or it may give rise to metastases which terminate life whilst the primary growth remains small. Metastasis may take place to the regional lymph glands or to the skeleton. The sternum, ribs, vertebral column and skull are the bones commonly involved.

The microscopic appearance of the malignant adenoma varies greatly, both in different specimens and in different parts of the same specimen. Most often the appearance is that of cubical or low columnar cells arranged in acini, whilst in places the cells may be disposed in solid masses or present a papillary formation. In some tumours there are areas resembling normal or hypoplastic thyroid tissue, or areas with the appearance of foetal adenoma or colloid adenoma.

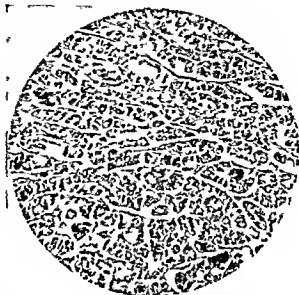


FIG 201 Malignant adenoma of the thyroid gland  
(Laboratory of Royal College of Physicians of Edinburgh)

**Papillary Adeno-carcinoma.** This tumour, which is the commonest type in Great Britain, is believed to develop generally in an adenoma or simple cyst. Occasionally it has been found in the posterior triangle of the neck, where it is believed to have originated in an aberrant nodule of thyroid tissue. The tumour generally attains considerable size and is soft, partly cystic, with a yellowish grey cauliflower appearance on section. Since at first it lies within the capsule of the original lesion it is less malignant than the other types. Eventually it gives rise to secondary growths in the regional lymph glands, but it rarely metastasizes to more distant sites.

Microscopically, it is composed of branching papilliferous processes supported by a well formed and vascular stroma, the cells are arranged in one or more layers and may be of a high columnar order, cubical, flattened or syncytial.

**Scirrhus Carcinoma** Unlike other types, this tumour commonly arises in a normal thyroid gland. It forms a small hard infiltrating growth which spreads diffusely by direct extension and invades adjacent structures, especially the larynx, trachea and infrahyoid muscles. At

an early stage it metastasizes to the lymph glands of the neck and mediastinum

Microscopically it consists of solid clumps of cells, small polyhedral or even spindle shaped, set in a fibrous tissue stroma. In some cases the growth is exceedingly cellular and may resemble a sarcoma

**Epidermoid Carcinoma** This tumour resembles the scirrhous

carcinoma, but is characterized microscopically by the presence of cells of squamoid pattern. It seems likely that many tumours formerly included in this type were carcinoma originating in the pharynx and involving the thyroid by contact spread

**Sarcoma** It seems probable that many tumours formerly included in this group were anaplastic forms of carcinoma. True sarcoma of the thyroid gland is now regarded as a very rare growth

**Pathological Effects of Carcinoma of the**

**Thyroid** There are no characteristic early symptoms and signs of malignant disease of the thyroid and this accounts for the frequency with which the disease may not be diagnosed clinically, but is recognized only on histological examination. While a malignant adenoma is still encapsuled diagnosis is scarcely possible

Progressive or rapid increase in size of a thyroid gland which has already been enlarged but stationary is often an important sign. A very suggestive sign is the sudden onset of hoarseness or aphonia. Pain referred to the side of the neck or the head though not pathognomonic is an important symptom. When the tumour has penetrated the capsule of the thyroid, especially if this occurs in the medial aspect of the gland the larynx and trachea are involved and become fixed, and the trachea may be displaced, compressed or even invaded. The infrahyoid muscles and later the skin become involved in the growth. One or both recurrent laryngeal nerves may be paralysed. Involvement of the pharynx and œsophagus is a not unusual feature and accounts for the dysphagia which is fairly common in this disease. It is very rare for a simple goitre to produce dysphagia, and therefore this symptom, in association with a thyroid enlargement, should arouse a suspicion of malignancy



FIG. 202. Malignant adenoma of the thyroid gland. Solid masses of malignant cells are seen invading an area of normal thyroid tissue.

(Department of Pathology University of Glasgow.)

In the late stages the skin is puckered and reddened, the superficial veins are engorged, and there is extreme dyspnoea, but cachexia, commonly seen in cancer in other regions of the body, is often absent.

**Metastases in Carcinoma of the Thyroid.** Next to the regional lymph glands the lungs are the commonest site of metastases. They are also common in the bones, especially in the vertebræ, the skull, and the long bones (*see* p 178). In a number of cases in which osseous metastases are present the primary growth is very small or of very slow growth, and in such cases the metastasis may be mistaken for a primary tumour.

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## CHAPTER XXI

### DISEASES OF THE PARATHYROID GLANDS

#### ANATOMY AND PHYSIOLOGY

THE parathyroid glands are yellowish brown ovoid or lenticular structures, measuring 5 to 7 mm in length and 1 to 2 mm in thickness. Normally there are two pairs of parathyroids, superior and inferior, but one parathyroid is absent in 24% of subjects, two are absent in 5% and occasionally only one is present.

Supernumerary parathyroids are fairly common and as many as twelve may be present. The parathyroids vary in position as well as in number. Usually they lie outside the capsule of the thyroid gland. The superior one is situated on the posterior surface of the lateral lobe, about its middle. The inferior one is larger than the upper and usually lies on the postero-medial aspect of the inferior extremity of the thyroid. The blood supply is usually derived from the anastomotic vessel connecting the superior and inferior thyroid arteries, and this vessel furnishes the best guide to them. In rare instances a parathyroid gland may lie buried within the substance of the thyroid gland. One of the superior parathyroids may lie behind the pharynx or the oesophagus, or in the areolar tissue at the side of the larynx, above the level of the thyroid gland. One of the inferior parathyroids may lie near the bifurcation of the common carotid artery, behind any part of the thyroid gland on the side of the trachea, or in the superior mediastinum close to the thymus or within it.

The parathyroid glands are composed of compact masses of epithelial cells separated by strands of areolar tissue containing vessels which tend to assume sinusoidal characters. The epithelial cells may vary in appearance according to the age of the subject. Usually they are polygonal and of moderate size with an abundant clear cytoplasm, the cell nucleus is usually eccentric and contains one to six nucleoli. After the age of ten years slightly larger cells are present either singly or in groups, they contain granules which are markedly acidophilic. It is not known which type of cell gives rise to the active secretion. Later in life vesicles containing colloid material are sometimes present. The colloid material, which does not contain iodine is more abundant after thyroidectomy.

The function of the parathyroid glands is to regulate the calcium and phosphorus metabolism of the body. The method by which the glands maintain a balanced ratio between intake, storage, utilization and excretion of calcium is very complicated and is influenced by many accessory factors such as diet, adequate quantities of vitamin D, and a proper amount of phosphatase in the tissues. Upon the correct metabolism of calcium depends the growth and stability of the skeleton, the



irritability of muscles and nerves and the coagulability of blood. The skeleton, being the reservoir for calcium in the body, is especially subject to the hormone effects of the glands, and in pathological conditions this source of calcium seems to be more readily available for assimilation by the tissues than the calcium absorbed by the bowel.

The amount of calcium in the blood remains very constant and is normally between 9 and 11 mg per 100 c cm of blood serum. The manner in which calcium is held in solution in the blood plasma is twofold. Part, about 2.5 to 4.5 mg, is held by adsorption with protein and is non-ionized and physiologically inactive. The remainder is present as ionized calcium, about 1 to 2 mg of which is dissolved as it would be in saline solution, and the rest (nearly half) is held in solution by parathormone. The method by which the hormone controls the solution is not fully understood, but when the parathyroid glands are excised it is this last fraction which disappears. There is a reciprocal relation between the concentration of calcium and phosphorus in the blood plasma whereby the acid base metabolism of the body is maintained, so that if the concentration of one rises that of the other falls.

After removal of the parathyroid glands the blood calcium may fall as low as 6 mg per 100 c cm (*hypocalcæmia*), and the reduction is associated with characteristic clinical features known as *tetany*. The features of tetany are abolished by the administration of calcium salts. Conversely, in certain states of over activity of the parathyroid glands the blood calcium is raised (*hypercalcæmia*), sometimes to as much as 18 to 28 mg per 100 c cm, with a proportionate fall in the blood phosphorus to as low as 1 mg per 100 c cm, and a greatly increased output of both calcium and phosphorus in the urine.

The isolation by Collip in 1924 of an active extract of the parathyroid glands afforded new avenues for the study of the parathyroid glands in relation to calcium metabolism. Continued injection in growing animals is followed by a considerable rise in the blood calcium and an increased excretion of calcium and phosphorus in the urine. The plasma phosphatase is always increased. The first effect of parathormone is to lead to an increased elimination of phosphorus by the urine, followed by increase of serum calcium made available by the reserves in the skeleton. The excess of calcium is excreted by the kidney and a progressive depletion of the mineral calcium of the skeleton occurs, resulting in rarefaction of the bones. There may be an associated loss of appetite, drowsiness, muscular atonia, and great dehydration. Metastatic calcification may occur in the kidneys, lungs, myocardium and gastro intestinal tract. These biological effects of excessive doses of parathormone have their counterpart in generalized osteitis fibrosa (*see p 150*).

## SYNDROMES OF PARATHYROID DISEASE

### Hypoparathyroidism

Parathyroid deficiency is manifest in its most characteristic form as post-operative tetany, following operations on the thyroid gland; but it may occur spontaneously.

**Post operative Hypoparathyroidism (*tetania parathyreopriva*)** Post operative tetany is an occasional complication after thyroidectomy. Fortunately in most cases the tetany is of a temporary character, and is due probably to temporary suppression of secretion caused by reactionary oedema in the glands. Complete removal of the parathyroid glands is followed by a rapid fall in the serum calcium to 2 or 6 mg per 100 c cm and then tetany usually appears within two to four days of operation. Tetany occurs frequently after removal of a parathyroid tumour generally it is transient but it may be complete and prove fatal.

It is supposed that half the parathyroid tissue normally available should be left to prevent tetany. Administration of parathormone restores the serum calcium to the normal level, and has been used successfully to counteract the symptoms of tetany. Calcium chloride injected intravenously has the same effect and acts more rapidly.



FIG. 203 Characteristic attitude of hand in tetany

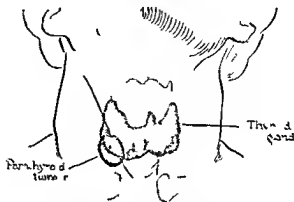
Parathyroid extract given over long periods may lose its effect and in such cases vitamin D in the form of Calciferol is effective.

The hypocalcaemia of parathyroid origin is associated with retention of calcium and phosphorus in the body and is not due to depletion by urinary excretion. Probably in the absence of parathyroid hormone the tissues are unable to utilize the calcium in circulation and storage in the skeleton results.

**Spontaneous Hypoparathyroidism** It is characterized by weakness sometimes by opacities in the lens, brittleness and ridging of the nails and loss of hair and dental enamel. The serum content of calcium is low. The condition is relieved by the administration of parathyroid extract or irradiated ergosterol etc.

The idiopathic tetany of childhood, which commonly occurs during the active stages of rickets, is associated with a low calcium content of the blood serum. The parathyroid glands often show enlargement in rickets and probably this is of a compensatory nature to overcome the effects of deficient absorption of phosphorus.

Tetany may result from continued vomiting, *e.g.* in pyloric or high intestinal obstruction, or it may follow the administration of alkalis *e.g.* in the treatment of peptic ulcer or pyelitis. The tetany in such cases is not associated with any alteration of the serum calcium nor related to parathyroid disorder, but is due to alkalosis which causes a decrease of the available calcium existing as free ions.



### Hyperparathyroidism

The association between hyperfunction of a parathyroid tumour and generalized osteitis fibrosa is now established and it is beyond doubt that the parathyroid activity is primary and the skeletal changes secondary.

FIG. 201 Adenoma of parathyroid gland in case of osteitis fibrosa



FIG. 202 Fractures of the femur in association with hyperparathyroidism

The parathyroid enlargement is usually confined to one gland less often to part of two glands. In rare cases there is overgrowth of all glands a feature which suggests an indirect hormonal effect probably from the pituitary. The degree of enlargement varies but on an average, it is three to eight times the normal before serious symptoms occur. Usually exploratory operation is required to demonstrate the enlargement. In many instances the enlarged gland has been abnormally situated *e.g.* in or deep to the thyroid gland in front of or behind the oesophagus or in the mediastinum.

The mechanism by which parathyroid over activity leads to the skeletal dystrophy is discussed on p. 151. Apart from the bone changes there may be other effects such as muscular hypotonia gastro-

intestinal disturbances, impaired renal function, abnormal deposition of calcium and a liability to the formation of renal calculi. Occasionally the serum calcium is normal but the urinary calcium is always increased.

unless as a result of anorexia the intake of vitamin D has been deficient.

After removal of a parathyroid adenoma the blood calcium and phosphorus promptly return to normal levels. There is usually relief from subjective symptoms, such as bone pains, and spontaneous fractures may heal and osteoclastic tumours disappear. Restitution of the skeletal density is usually progressive, especially in young subjects. Urinary calculi may disintegrate or require removal.

Tetany, sometimes fatal, may develop after operation, even when the blood calcium is as high as 10 mg. per 100 c.cm.

While hyperparathyroidism is usually due to a tumour of a parathyroid gland, there is another type of disease in which the parathyroid glands are hyperplastic as a secondary manifestation *e.g.*, in osteomalacia, and in chronic renal failure, especially in childhood. It is probable that in such cases the parathyroid overgrowth is due to acidosis with retention of phosphorus. The differential diagnosis from parathyroid osteitis may then be difficult but usually the blood level of phosphates (low in osteitis fibrosa, high in secondary hyperparathyroidism) makes the situation clear.

### TUMOURS

Tumours of the parathyroid glands are rare, but they are of great interest because they are often, though not always, associated with

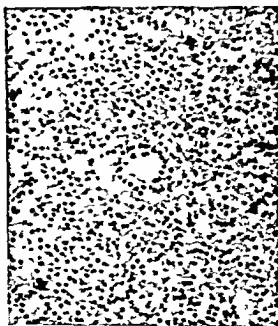


FIG. 206. Adenoma of parathyroid gland. There are solid masses of large clear cells with dark staining nuclei. In addition, acini are seen lined by clear columnar cells.

(Laboratory of Royal College of Physicians of Edinburgh.)

hyperparathyroidism There are two varieties—adenoma and carcinoma

*Adenoma* As in many other glandular organs there is not always a sharp distinction between hyperplasia and adenoma Usually the adenoma is single yellow or greyish white encapsulated and lobulated large examples (with dimensions of  $7.5 \times 5 \times 1.8$  cm have been encountered) though often not detectable The tumour may be cystic and there may be areas of calcification in it

Microscopically a parathyroid adenoma is composed of interlacing compact cords or masses of large clear cells uniform in type and separated by vascular spaces (see Fig 206) The stroma is usually scanty In some examples the cells may in parts be arranged in acini containing colloid like material

*Carcinoma* This is a very rare tumour it may arise spontaneously or from an adenoma The tumour which grows rapidly and irregularly, may reach the size of a fist or larger It infiltrates the thyroid gland the muscles and the trachea and larynx and there is a great tendency to local recurrence after operation Metastases occur in the lymph glands the lungs and the skeleton Histologically the tumour is composed of irregularly disposed cells of various sizes The cell nucleus is often large and commonly shows mitosis

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## CHAPTER XXII

# DISEASES OF THE PHARYNX, LARYNX AND ŒSOPHAGUS

### PHARYNGEAL DIVERTICULUM

A DIVERTICULUM of the pharynx originates as a protrusion of the mucous membrane through the posterior wall of the pharynx in the middle line. The site of origin of the pouch is constant, and is determined by the arrangement of the muscle fibres at the entrance to the œsophagus. The inferior constrictor muscle of the pharynx consists of two portions each with a different disposition of fibres, and a different action. The upper fibres (thyropharyngeus) take origin from the thyroid cartilage and pass obliquely upwards and backwards round the pharynx to its median raphe. The lower fibres (cricopharyngeus) arise from the cricoid cartilage and encircle the entrance to the œsophagus like a collar. Posteriorly, between the two parts of the inferior constrictor, the wall of the pharynx is potentially weak and under abnormal conditions constitutes an area of lessened resistance. On the pharyngeal surface this area may be marked by a small depression which has been called the 'pharyngeal dimple' although it is rarely detectable in normal subjects. When a diverticulum of the pharynx occurs it is between the two sets of fibres of the inferior constrictor muscle.

**Ætiology.** There is no evidence that a diverticulum at this site is congenital in origin for its occurrence in young subjects is unknown apart from organic stenosis of the upper part of the œsophagus. Most examples of pharyngeal diverticulum have been found in adults past middle life, and the incidence is greater in males than in females (3:1).

The determining cause of the diverticulum is accepted to be interference with the normal co-ordination of the act of swallowing whereby intrapharyngeal tension, generated during deglutition is unduly prolonged. *The importance of this factor is suggested by the long history of dysphagia even though there may be long intermissions.* The mechanism of swallowing can be observed on pharyngoscopic examination or in cases of suicidal cut throat, and it is then seen that the upper orifice of the œsophagus relaxes only for a brief interval after contraction of the detrusor muscles above it, and that when saliva or a bolus of food has been transmitted it closes at once. Keith measured the pressure generated in the pharynx on deglutition and found it rose to a maximum of 45 mm. of mercury, such intermittent pressure, if unduly sustained, would doubtless produce strain at the point of obstruction. In the production of a diverticulum it is believed that there is some degree of neuromuscular incoordination in the act of swallowing by which the cricopharyngeus muscle fails to relax in

normal sequence to the contraction of the pharyngeal muscles above it (achalasia) and that by repetition of intermittent impulses of high pressure, the least supported area of the pharynx (especially if already weakened in age) gradually stretches. Once formed the hernial protrusion increases in size progressively by the weight of its contents, the displacement forwards of the upper aperture of the œsophagus renders more difficult the passage of food into the œsophagus and the propulsive force of the pharynx is expended in dilating the sac. It is for this reason that no food enters the œsophagus until the diverticulum



FIG. 207 Pharyngeal diverticulum

is filled. A pharyngeal diverticulum has been observed in association with goitre, and the pressure exerted by the enlarged thyroid either on the œsophagus or the recurrent laryngeal nerves has been held responsible. A median diverticulum arising at the lower end of the pharynx and protruding between the œsophagus and trachea has been described.

**Anatomical Relations and Structure of the Diverticulum.** A pharyngeal diverticulum when small retains a partial covering of muscle fibres acquired from the inferior constrictor. With increase in size of the pouch the muscular coat becomes gradually attenuated, until finally muscle fibres are present only at its neck. The pouch is

usually flask shaped, in a very few instances the fundus is bifid. The pouch descends behind the œsophagus, situated in the space between the pretracheal and prevertebral fasciæ, and, when large, the fundus may reach the superior mediastinum (see Fig 207). In some cases the diverticulum presses upon and leads to atrophy of the posterior wall of the œsophagus. The diverticulum is usually inclined to one or other side, generally the left, and after a meal a swelling, which gurgles, may be obvious in the posterior triangle of the neck. The dragging effect of the diverticulum brings its mouth into the same axis as the pharynx and the entrance of the œsophagus appears as a narrow aperture at the anterior border of the neck of the sac. The orifice of the diverticulum is circular or elliptical. Examination after an opaque meal demonstrates the size of the pouch and how it must fill before food can enter the gullet.

The wall of the pouch varies in thickness in different specimens. It is lined with squamous epithelium which may be smooth or rugose, and which may undergo ulceration or hyperkeratosis. A muscularis mucosæ may or may not be present. The outer fibrous coat, which makes up most of the thickness of the wall of the pouch is derived from the pharyngeal aponeurosis. This coat is separated from the submucosa by thin areolar tissue, which may afford a plane of cleavage in operating.

Stagnation of food and saliva may lead to ulceration of the interior of the diverticulum and may cause perforation or abscess formation in the neck or mediastinum. Emaciation often ensues from the prolonged difficulty in swallowing. Aspiration pneumonia from regurgitation of the stagnant contents of the sac is not an infrequent cause of death. Occasionally a carcinoma has taken origin inside a diverticulum.

#### Lateral Pharyngeal Diverticulum

This variety of diverticulum is of developmental origin. It is thin walled and deeply situated, and has usually a communication with the tonsillar or the pyriform fossa and sometimes with the skin surface. It is lined by squamous epithelium. Distension within its cavity may lead to severe pressure effects.

#### LARYNGOCELE (Cervical Aerocele)

This is an air containing sac which results from herniation of the mucous membrane of the larynx through a defect in the laryngeal skeleton. A similar condition is normally found in a high state of development in some of the higher apes.

Laryngocele may arise in children, but more often it occurs in adults as a result of chronic expiratory obstruction. It is seen in glass-blowers, players of wind instruments, and sufferers from chronic cough. Two types are recognized—internal and external laryngocele.

Internal laryngocele results from dilatation of the "saccus laryngis" at the anterior end of the ventricle of the larynx. It presents a tense swelling above one vocal cord, and may cause dysphonia or even dysphagia.



External laryngocele is due to protrusion of the mucous membrane through the thyro hyoid membrane. It gives rise to a painless swelling in the neck, which enlarges on forced respiration and empties with a gurgle either spontaneously or on pressure. The cyst tends to increase in size gradually and may reach as far as the clavicle. It may be bilateral.

## CARCINOMA OF THE PHARYNX AND LARYNX

In the pharynx there are two common starting points for cancer—(1) at the upper aperture of the larynx (epilaryngeal growths) and (2) at the narrow or tubular part of the pharynx behind the cricoid (hypopharyngeal growths). The growths are of the nature of squamous cell carcinoma, in which cell nest formation usually is present. Occasionally a basal cell type of growth occurs, and sometimes the tumour has an abundant lymphoid stroma (lympho epithelioma).

**Epilaryngeal Growths** Epilaryngeal growths are commoner in men than in women and occur most often after the age of fifty years. The growth generally takes the form of a raised ulcer, sometimes papillary types occur, but less often than at other sites in the pharynx. There are four common starting points for the growth: (1) The epiglottis (2) The ary epiglottic fold, i.e., in the medial wall of the piriform recess (3) The floor of the piriform recess, and (4) The lateral wall of the piriform recess. Growths of the epiglottis tend to spread to the valleculæ and to invade the base of the tongue. The epiglottis may be entirely destroyed. Growths of the ary epiglottic fold may extend into the interior of the larynx and towards the lateral wall of the pharynx. Growths on the floor of the piriform recess are situated most unfavourably, because gradual spread to the larynx is of common occurrence. In some instances the tumour in the piriform recess remains very small and no large glandular metastasis appears below the angle of the mandible. The swelling in the neck may be explored and its primary origin overlooked.

The effects produced by epilaryngeal growths are generally different from those at other sites in the pharynx. Tickling in the pharynx, the sensation that a foreign body is lodged there, and discomfort in swallowing saliva apart from food are usually the earliest evidence, and pain and hoarseness are of later occurrence. On laryngoscopic examination the growth can usually be seen and it is often covered by rather tenacious exudate, which may be blood stained. It is characteristic that the exudate is not readily dislodged in making swallowing movements. The cartilages at the upper aperture of the larynx tend to become fixed, and the surrounding mucous membrane is often oedematous and congested. Involvement of the cervical lymph glands cannot on the whole be regarded as either an early or a conspicuous feature of epilaryngeal growths with the exception of growths of the piriform recess.

**Hypopharyngeal Growths** (Post cricoid cancer) Hypopharyngeal growths are especially common in women and quite frequently they occur before forty years of age. As emphasized by Logan Turner,

many subjects who develop cancer at this site have for years suffered from intermittent difficulty in swallowing of nervous origin

The common starting points are the lateral or posterior walls of the lowest part of the pharynx. The growth generally takes the form of a slightly raised papillary excrescence of roughly circular outline. It tends to encircle the pharynx and to extend to the laryngeal cartilages, especially upwards to the arytenoids. At a later stage extension to



FIG 208 Radiogram of thorax in a case of post-ericoid cancer in a man aged seventy-one years. The trachea and bronchi contain barium as a result of regurgitation. Death due to long delayed septic bronchopneumonia.

the thyroid gland is common. The lymph glands in one or both posterior triangles may be invaded. A growth situated at the junction of the pharynx and oesophagus may extend for a considerable distance down the gullet. When that happens it may perforate the trachea and produce a fistula.

Growths in the lowest part of the pharynx are too distant to be seen by laryngoscopic examination, but suggestive signs are oedema and fixation of one of the arytenoid cartilages and stagnation of exudate. In the advanced stages it may be impossible to state from what point the growth originated. It may displace the larynx forwards, or may be

palpable in the neck. From perforation, an abscess may form in the neck or in the mediastinum. A common cause of death is septic pneumonia as a result of regurgitation of food into the larynx owing to obstruction at the entrance of the œsophagus (Fig. 208).

**Intrinsic Carcinoma of the Larynx.** Intrinsic carcinoma of the larynx usually begins in one of the vocal folds, much less often in one of the ventricular folds and very rarely in the subglottic region. The usual site of origin is the anterior half of the vocal fold at its free border, from which the tumour tends to spread forwards and to the opposite vocal cord. The growth is usually of a warty or cauliflower type and has the histological characters of a squamous cell carcinoma.

It is characteristic of intrinsic cancer of the larynx that it grows slowly, and many years may elapse before the larynx is extensively invaded. Metastases occur in the glands around the carotid sheath. Recurrence of disease in these glands is common after operation.

Intrinsic cancer of the larynx is rare before the age of fifty years, and is more than ten times commoner in men than in women. The chief effect of the growth is to lead to changes in the voice, but at a later stage it may give rise to aphonia, dyspnoea and stridor, and if neglected to death from hæmorrhage, asphyxia or septic pneumonia.

## SPASM AT THE ENTRANCE OF THE ŒSOPHAGUS

This is a common cause of dysphagia. Its underlying cause is spasm of the cricopharyngeus part of the inferior constrictor muscle. It occurs most often in neurotic subjects, especially middle-aged anæmic women, and is generally of long duration before it comes under observation. In rare cases the muscle is greatly hypertrophied.

The appearances noted at the lower part of the pharynx are fairly constant and characteristic. The mucous membrane, instead of being disposed in stellate folds that separate readily, presents a drawn and irregular appearance. The œsophageal orifice is small, often excentric, and may be slit like, it is readily fissured and, therefore, if a bougie is passed it must be done carefully. Brown Kelly noted that anæsthesia did not bring about relaxation of the spasmodic contraction, but that dilatation effected relief.

In subjects of this disorder the mucous membrane of the mouth and pharynx generally undergo changes. The tongue is abnormally smooth from atrophy of its filiform papillæ and may show fissures or leukoplakia. The cheeks and palate are dry and have a waxy pallor. Saliva is usually scanty but may be excessive.

In many instances fine epithelial webs develop in the hypopharynx and may aggravate dysphagia.

Anæmia is often associated with this condition and recent observations suggest that relief may be gained by full doses of iron and an adequate diet, provided obstruction is overcome.

Nervous difficulty in swallowing, especially in women, has preceded cancer of the pharynx or the œsophagus in a large proportion of cases. Possibly the growth arises as a result of chronic irritation caused by the functional incoordination or the nutritional deficiency.

## CONGENITAL ABNORMALITIES OF THE ŒSOPHAGUS

At about the third week of development of the embryo the œsophagus is represented merely by an annular constriction between the pharynx and the stomach, and it is only after elongation of the neck and the growth of the lung buds that it becomes tubular. In the early stages of development the cephalad part of the œsophagus and the trachea form a single short canal, and later the two tubes become separated by

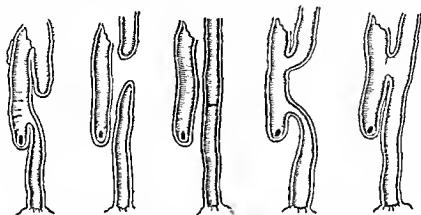


FIG. 209. Diagrammatic representation of congenital abnormalities of the œsophagus and trachea. The third figure depicts an occluding diaphragm of mucous membrane. (After Vincent.)

the ingrowth of a longitudinal septum from each side, which completes the partition. The caudal part of the septum is the last to be completed.

As the œsophagus and trachea have a common origin it is not surprising that sometimes fistulous channels persist. Such congenital maldevelopments are generally incompatible with life. The communication is commonest with the trachea at its bifurcation or with the right bronchus. In some instances the œsophagus and trachea communicate at two points and a segment of the œsophagus is absent. The other abnormal connexions of the œsophagus and trachea are depicted diagrammatically in Fig. 209.

Congenital maldevelopment of the œsophagus itself is of more importance than trachœo-œsophageal fistulæ because it is often compatible with life, and may be a cause of dysphagia in childhood. The chief types are (1) congenital narrowing of the whole œsophagus, (2) congenital stenosis of the upper or the lower end, (3) absence or narrowing of a segment, (4) an occluding diaphragm of mucous membrane, and (5) congenital shortening.

Congenital narrowing of the œsophagus may be so extreme that the organ is represented merely by a fibrous cord, but in many instances the œsophagus is properly developed, but in miniature. The recognition of congenital constriction of the œsophagus in infancy depends on the degree of obstruction. If the stenosis be complete all food is regurgitated,

but in many cases narrowing causes no symptoms as long as the diet is fluid. In a few cases a congenital web of mucous membrane has been recognized by œsophagoscopy and has been successfully perforated.

In *congenital shortening* (which is a comparatively rare condition) the œsophagus ends about the level of the eighth thoracic vertebra. A portion of the stomach is therefore held suspended in the posterior mediastinum above the hiatus in the diaphragm (thoracic stomach). The importance of this developmental abnormality is its simulation of parœsophageal hernia as well as certain types of cardiospasm.

Ulceration of an intractable kind is particularly liable to occur at the junction of the œsophagus and the stomach (*see p. 452*).

### Œsophageal Diverticulum

Diverticula of the œsophagus are rare and unimportant as they are seldom discovered during life and rarely give rise to symptoms.

It is customary to describe three varieties: (1) congenital or developmental, (2) traction, and (3) pulsion diverticulum.

(1) A small diverticulum may result from imperfect separation of the trachea and œsophagus. It occurs usually in the anterior wall of the œsophagus about the bifurcation of the trachea and is firmly incorporated with the membranous wall of the trachea. The pouch is covered at its neck and sides by muscle bundles derived from the œsophagus.

At or about the level of the bifurcation of the trachea developmental defects in the œsophageal musculature are common and through these small diverticula may emerge. The muscular defects probably represent incomplete coalescence of the relatively thin striated muscle fibres of the upper part of the œsophagus with the stouter plain muscle of the lower part.

(2) A traction diverticulum is usually situated in the neighbourhood of the bifurcation of the trachea or where the left bronchus crosses the œsophagus, and usually owes its origin to adhesion of enlarged tuberculous glands to the wall of the œsophagus. Less often adhesion of the pleura or the pericardium to the œsophagus may be the cause. The movements of respiration and deglutition exert a gradual dragging on the walls of the œsophagus so that finally they may be drawn out in the form of a funnel or diverticulum. Such a diverticulum is usually wide mouthed and of small size and more than one may be present. As a traction diverticulum is wide mouthed and as the fundus is often situated at a higher level than its entrance food does not tend to stagnate. Perforation by a foreign body lodged within its cavity has been recorded.

(3) Pulsion diverticula are very rare. A variety known as *epiphrenic* sometimes occurs in the lower part of the œsophagus on the left side. It consists of a protrusion of the mucous membrane through the longitudinal muscle fibres of the œsophagus. The communication with the œsophagus may be very minute so that the pouch may become greatly distended with mucoid fluid.

Occasionally pouching and diverticulum formation occur immediately above an old standing fibrous stricture.

## CARDIOSPASM ACHALASIA OF THE ŒSOPHAGUS

This condition is characterized by dilatation and hypertrophy of the œsophagus associated with a peculiar type of obstruction at its lower end. It affects women slightly more often than men, and it begins insidiously and progresses slowly or intermittently during many years. It is rare in childhood, it generally occurs between the ages of twenty five and forty five years, but it may not be present till old age. Symptoms sometimes appear for the first time after a debilitating illness.

The obstruction at the lower end of the œsophagus is usually associated with no obvious organic lesion and appears to be due to functional constriction. It gives rise to difficulty in swallowing at first slight and intermittent, later severe and constant. The obstructed œsophagus dilates, and foodstuffs and fluid, denied egress at the cardia, stagnate and ferment or else are regurgitated. In the later stages the constant obstruction leads to starvation and emaciation.

**Pathological Features** In an advanced case the œsophagus is lengthened by 3 cm or more, it is greatly dilated and attains a circumference of even 15 cm. Usually the dilatation is most obvious in the lower two thirds. Inferiorly, the dilatation usually reaches only to the diaphragm, superiorly, in long standing cases it may extend as far as the cervical portion or even to involve the pharynx. The dilatation varies in shape—elongated fusiform or flask shaped—or, if greatly lengthened, it may assume a sigmoid outline.

In addition, the œsophagus shows considerable muscular hypertrophy, the muscular coat being increased in thickness from the normal of about 1.5 mm to as much as 4 mm or even 7 mm. The hypertrophy, unlike that in simple stricture in which both sets of fibres participate equally, is due usually to overgrowth of

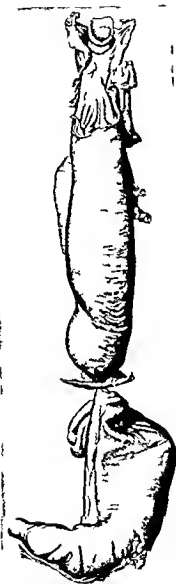


FIG. 210 Œsophagectasia. Note the extreme dilatation of the œsophagus and the hypertrophy of the circular muscle. The dilatation stops abruptly at the hiatus in the diaphragm. (Museum of Royal College of Surgeons of Edinburgh.)

sets of fibres participate equally, is due usually to overgrowth of

the circular muscle, but in exceptional cases only the longitudinal fibres are affected.

The mucous membrane, stretched and thinned, may undergo various secondary changes, such as inflammation and ulceration, and, as a result of chronic inflammatory changes, may later become thickened and form multiple polypoidal overgrowths.

Particular interest attaches to the pathological changes in the lower end of the œsophagus, and in regard to these there are many conflicting observations. Most observers are agreed that there is, during life, undue narrowing of the œsophagus at the diaphragm, and that usually there is no organic lesion to

which the narrowing may be attributed. The muscle of the œsophageal wall, except in rare cases, is not hypertrophied at the point of narrowing compared with above, nor is there usually any fibrous stricture, and, indeed, in contrast to the dilatation and hypertrophy higher up, the lower end of the œsophagus is almost normal in appearance. In advanced cases there is sometimes considerable diffuse fibrosis which may lead to organic stenosis at the lower end of the œsophagus. Examination during life by means of bougies or



FIG. 211. Cardiospasm; it occurred in a woman aged twenty-one years, and dysphagia had been present since childhood. The œsophagus is elongated and tortuous.

the œsophagoscope has yielded contradictory evidence, for whereas some observers have found the lower end of the œsophagus constricted and spastic, others maintain that it is opened and closed on respiration just as in the normal subject. When palpated by the finger during gastrotomy the lower end of the œsophagus feels somewhat tight and it yields only gradually to dilatation. Radiographic examination after the administration of opaque fluid shows that obstruction occurs within the diaphragmatic aperture, and that the stomach immediately below is healthy. Sometimes from the weight of the contained fluid the lower part of the œsophagus sinks below the level of the œsophageal opening in the diaphragm, and then the conical outlet appears to lead from the side of the œsophagus a short distance from its lowest point. A residue of the opaque medium may be observed several

hours after its ingestion. Intermittent vigorous contractions of the œsophagus are obvious on fluoroscopic examination.

**The Cause of the Disease** Since Hannay, in 1833, first described its principal features, there have been many views as to its causation, and only recently has its ætiology been made more clear. Formerly its origin was attributed to such factors as congenital malformation, phrenospasm and spasmodic contraction of the hypothelial cardiac sphincter (cardiospasm).

The view now held is that the dilatation and hypertrophy develop gradually and are for a time a result mainly of functional obstruction due to achalasia or lack of relaxation of the lower end of the œsophagus. The œsophagus, like the remainder of the alimentary tract, is supplied by sympathetic and parasympathetic fibres. The sympathetic fibres reach the lower end of the œsophagus *via* the thoracic sympathetic chain, the splanchnic nerves, and the coeliac plexus (alongside the left gastric artery); the parasympathetic fibres are from the vagi.

### ULCERS IN THE ŒSOPHAGUS

Ulceration of the mucous membrane of the œsophagus may result from the abrasion by a foreign body, careless instrumentation or burning by corrosive fluids. Following wasting diseases, so-called decubitus ulcers have been found at post mortem at the upper end of the œsophagus.

**Peptic Ulcer** Most interest is attached to peptic ulceration of the œsophagus which affects the lower third. The disease occurs chiefly in adults, but occasionally develops in childhood. In many instances gastric or duodenal ulceration coexists.

Those who have made a detailed study of peptic ulceration find that the appearances and changes vary according to its degree of activity, its duration and the presence of secondary pathological developments. In many there may be only œsophagitis, in others there is a single ulcer or extensive denudation, and finally the ulcer may be chronic and may culminate in fibrous stenosis. The appearance of the ulcer is similar to that of peptic ulcer elsewhere; perforation and hæmorrhage are rare, but may be fatal.

In association with peptic ulcer of the œsophagus there are various associated pathological changes which may have a bearing on its origin and behaviour. The œsophagus is reduced in length and it is found that in the absence of stenosis an instrument passes the cardia with unusual ease. A trans-diaphragmatic herniation of the stomach of varying degree is present. These features are so constant that Allison believes they provide the key to the causation of ulceration at this site. There is evidence that the diaphragmatic hiatus may at any age become lax or liable to hernia (paraœsophageal hernia). In the commonest variety the cardia and a portion of stomach are drawn into the mediastinum partly by suction and to a less extent by traction following prolonged œsophagitis. As a result the normal check and release mechanism at the cardia is impaired, the cardiac orifice becomes patulous, and allows reflux of acid into the œsophagus and creates local conditions favourable



for ulceration. These changes are readily confirmed at operation although the œsophagus appears shortened and the stomach is partly in the mediastinum (provided there is no inflammatory fixation) the stomach is readily drawn back into the abdomen.

Peptic ulcer of the œsophagus is not only responsible for intractable dyspepsia but for dysphagia as well. Surgical treatment when required in the absence of stenosis is directed to the repair of the diaphragmatic defect.

## TUMOURS OF THE ŒSOPHAGUS

Simple tumours in the œsophagus are rarities. Those reported are submucous lipoma, fibroma and leiomyoma. They may be sessile or pedunculated, and may assume considerable length. The larger ones may cause obstruction of the œsophagus.

### Cancer of the Œsophagus

Carcinoma is much the most frequent cause of obstruction of the œsophagus. It is only during recent years that success on a considerable scale has followed surgical treatment. In a high proportion of cases the disease is advanced when first recognized and has led to such depletion that the patient is ill fitted to bear the burden of an extensive thoracic operation.

Like cancer of the mouth, cancer of the œsophagus may owe its origin in some measure to chronic irritation. Except in the cervical portion, where the sex ratio is about equal, the disease is much more common in men than women (5:1), therefore, tobacco juice, alcohol, excessively hot food, etc., have been held responsible for irritating the mucous membrane. The disease is commonest after the age of fifty. Leukoplakia of the œsophagus is commonly observed in old subjects, and its presence is often noted in the neighbourhood of a carcinoma, and, as in the tongue, it has been regarded as a precancerous condition. It cannot be claimed that syphilis has any relationship either through its systemic effects or by producing any local predisposition.

Statistics vary as to the frequency with which different parts of the œsophagus may be affected. Growths tend to appear with greatest frequency at those parts of the œsophagus that are subjected to narrowing by the arch of the aorta, the left bronchus, and the diaphragm. Without doubt the most common site is at the level of the arch of the aorta or just below it. Next in frequency is the lower part of the œsophagus, a few centimetres above the diaphragm, and that part may also be involved by carcinoma extending from the cardiac end of the stomach. Primary cancer in the cervical part is rare, but there may be extension from the pharynx. Dual growths have been met with in the œsophagus as in other parts of the alimentary canal. There is no evidence that the malignancy of carcinoma of the œsophagus varies at different levels.

**Types of Growth.** Cancer of the œsophagus presents itself in two common forms: (a) a flat ulcerating type of growth, (b) a polypoidal or cauliflower type. Intermediate types are quite common. In rare

cases an infiltrating scirrhus type that extends over a wide area of the gullet may occur

The majority of malignant growths of the œsophagus show the histological features of a squamous cell carcinoma, but keratinization and cell nest formation are usually lacking. Sometimes a glandular type of carcinoma is found, and it is believed to originate in the mucous glands although it has been suggested that heterotopic gastric mucosa or embryonic epithelium in the wall of the œsophagus may explain its occurrence. Basal cell carcinoma of undifferentiated type is met with in a considerable number of cases but, unlike the common basal cell carcinoma of the skin, it is always malignant.



FIG 212 Carcinoma of the distal part of the œsophagus

(Department of Clinical Surgery  
University of Edinburgh)

**Morbid Anatomy** At first the disease is confined to the mucous membrane and involves a limited area but by extension it gradually encircles the gullet. It is stated that the lumen may be reduced to 5 mm before dysphagia occurs. Longitudinal spread is slight in the scirrhus type, though in the cauliflower type it may be considerable. The ulcerating type causes local thickening of the œsophageal wall and has nodular, raised and everted edges of irregular outline. The older ulcerated portion is hollowed out and the wall of the œsophagus may be much reduced in thickness and thus lead to perforation. Polypoidal growths have a lobulated or villous appearance, with a friable surface that ulcerates and bleeds readily and when inspected is generally coated with a blood stained foetid discharge. Such a tumour produces obstruction by its bulk rather than by any changes effected in the wall of the œsophagus.

The œsophageal wall above a growth is redder than usual from increased vascularity and appears relatively immobile and stiffened. Patches of leukoplakia are commonly noted in the neighbourhood of the tumour. Hypertrophy of the muscle and dilatation of the lumen are rarely more than slight.

**Mode of Spread** Carcinoma of the œsophagus shows considerable variation in its rate of growth and dissemination. In

some the tumour may grow slowly during a period of a year or more without extending externally and without involvement of the

lymph glands, whereas in others it may involve a considerable part of the oesophagus and rapidly invade surrounding structures, or give rise to secondary deposits in lymph glands or even distant parts. Spread of the disease is mostly by direct extension and infiltration, when the muscular coat is penetrated local periesophagitis occurs and fixes the oesophagus to the mediastinal structures, which may later become involved in the growth. Lymph vascular spread is fairly common and is present in at least 50% of cases at autopsy. A growth in the cervical part of the oesophagus may cause enlargement of the cervical lymph glands on one or both sides. In the thorax the mediastinal lymph glands may be involved, and the glands at the cardia may be involved even though the tumour is in the midzone of the oesophagus. In growths at the lowest part of the oesophagus the celiac lymph glands have been found enlarged and there may be metastases in the liver. Distant spread by the blood stream is unusual, its occurrence has been noted as a result of invasion of the thoracic duct or of the pulmonary veins.

#### Complications

Many secondary complications may ensue when an oesophageal cancer spreads outwards or invades adjacent viscera. Acute perforation may occur, resulting in mediastinitis, and widespread



FIG 213 Radiogram of an early carcinoma of the oesophagus. The tumour was situated immediately below the arch of the aorta.

subcutaneous emphysema. Perforation is sometimes gradual and an abscess develops. Invasion of the trachea or a bronchus is of relatively frequent occurrence and leads to aspiration pneumonia. Penetration of the lung with resulting abscess or gangrene is a common terminal feature but invasion of the pleural cavity with resulting empyema is much less common. In the neck and the upper part of the thorax one or other of the recurrent laryngeal nerves may be involved in the growth. The left recurrent nerve is of greater length than the right and

consequently is more frequently implicated. Secondary involvement of the thyroid gland may result from a growth in the cervical part of the Œsophagus, and such an extension may be readily mistaken for a primary tumour of the thyroid gland.

When obstruction occurs there is progressive emaciation and dehydration, sometimes with much toxæmia. When the stomach is exposed at operation it is usually found to be smaller than normal from prolonged reduction in its activity.

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## CHAPTER XXIII

### DISEASES OF THE STOMACH AND DUODENUM

#### PHYSIOLOGY OF GASTRIC SECRETION AND MOTILITY

THE stomach has several functions. It acts as a mixing chamber for food, cools or warms it to the temperature of the body, renders it fluid for its passage along the intestine, and secretes pepsin and hydrochloric acid for the first stage of protein digestion. In addition, it produces an internal secretion concerned with hæmatopoiesis.

**Gastric Secretion** The acid secretion is produced by oxyntic cells in the simple tubular glands of the stomach wall, and, as Pavlov showed many years ago, the acid is produced in greatest amount at the cardiac end of the stomach, whereas the secretion is neutral or even alkaline near the pylorus.

Pavlov's studies of the secretion of isolated gastric pouches in dogs indicates that the rate of flow and acidity are influenced by nervous and chemical factors. The nervous stimulus, transmitted from the hypothalamus via the vagus nerves, is responsible for the "appetite" juice and may give rise to increased secretion in conditions of psychological stress. The chemical stimulus occurs when food enters the stomach and is believed to be due to a hormone "gastrin," elaborated in the pyloric region. It is believed that both nervous and chemical stimuli exert their effect through the agency of histamine, which is known to act directly on the parietal cells.

The concentration of hydrochloric acid at the point of secretion is maintained at a constant level of about 0.4%. Variations in acidity such as are seen on gastric analysis depend, on the one hand, on the volume secreted and on the other, on neutralization by saliva, food, mucus and the alkaline pyloric and duodenal juices.

In health, the acid level varies at different ages, being low in childhood, rising to a maximum in early adult life and thereafter gradually declining. Gastric achylia (histamine fast achlorhydria), is found occasionally in healthy young persons. According to Vanzant its frequency increases with age, particularly in women, and it may be found in as large a proportion as 28% in elderly women.

**Gastric Motility** The stomach is normally in a state of tone, the degree of which varies greatly, and is naturally greater in sthenic than in visceroprotic persons. The tone is interrupted at intervals by peristaltic waves which on the fluorescent screen, appear at about the mid point of the stomach and pass thence to the pylorus. The discharge of gastric contents begins soon after the meal reaches the stomach and should be completed in from three to five hours.

When the gastric motility is studied by means of a swallowed balloon registering through a tambour on to a kymograph drum,

long periods though demonstrably not healed. This may be due to the protection of the exposed nerve fibres by insensitive granulation tissue or adherent mucus. In such a phase even the administration of hydrochloric acid in considerable amount may fail to elicit pain.

### PEPTIC ULCER

Peptic ulcers may develop on any portion of the alimentary tract exposed to the action of the gastric juice. The great majority occur in the stomach and duodenum, and such gastric and duodenal ulcers will be described in detail in this chapter. It will not be out of place to mention, however, that peptic ulcers of similar type occur also in the distal portion of the œsophagus (*see* p. 452), in the jejunum after the performance of gastro jejunostomy (*see* p. 469), and rarely in other parts of the small intestines (*see* p. 502).

#### Acute Ulcer

It seems possible that all ulcers are at first acute. Acute ulcers may be single, but they are often multiple, and may occur in any part of the stomach or the duodenum. They arise from a variety of causes, and are common in the later phases of many acute infective and toxic conditions. The duodenal ulceration that follows extensive burns belongs to this category. Acute ulcers are round or oval, and at first they are mere erosions of the mucous membrane. If they extend they penetrate the deeper coats of the wall by progressive sloughing, which diminishes in extent as the ulcer deepens and gives the ulcer a characteristic terraced appearance. Acute ulcers are apt to erode arterioles, and to cause hæmorrhage. Less commonly they penetrate all the coats and perforate suddenly into the general peritoneal cavity. Microscopically, there is often a striking absence of inflammatory change, and apart from some œdema the surrounding wall may show little deviation from the normal.

The great majority of acute ulcers undoubtedly heal rapidly within a few weeks of their onset and do not recur. Only relatively few persist, but this small proportion of chronic ulcers forms the bulk of those seen by the surgeon.

#### Chronic Ulcer

Chronic ulcers show a remarkable tendency to be restricted to certain very limited regions in the stomach and duodenum. In the stomach the "ulcer bearing area" includes the smaller curvature and the adjacent anterior and posterior surfaces, from the œsophageal orifice to about  $1\frac{1}{2}$  inches from the pylorus, in the duodenum the area affected is  $\frac{1}{2}$  to 1 inch from the pylorus. It has been estimated that 90% of chronic ulcers are found in these situations. The pylorus itself is but uncommonly the site of ulceration (5% to 10%), and the great majority of so called pyloric ulcers are actually situated in the duodenum. The greater curvature, fundus and cardia are only very rarely affected.

Two or more chronic ulcers frequently coexist. "Kissing" duodenal ulcers are common, and coincident gastric and duodenal

ulcers are sometimes found. Failure to recognize such a coincident ulcer accounts for some of the unsatisfactory results of operation.

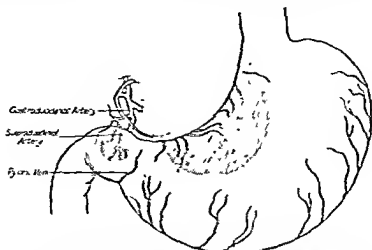


FIG. 214. Sites of peptic ulceration. The shaded portions indicate the sites of the great majority of peptic ulcers.

**Frequency and Incidence.** Peptic ulcer is a common disease in Great Britain, North America, Europe and certain parts of India.

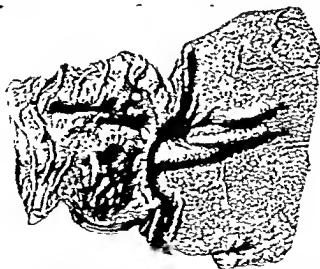


FIG. 215. Duodenal ulcers. Two ulcers, characteristically small and rounded, are situated on the anterior and posterior wall respectively, about 1 cm. beyond the pylorus. The anterior ulcer has perforated.

Elsewhere its frequency is less, while in some countries, notably China and Africa, it is said to be rare.

Peptic ulcer has not always been so common. There is a good deal of evidence, gathered mainly from statistics relating to perforation, to suggest that it was comparatively rare during the nineteenth century,

while as regard the recent past, both hospital records and the experience of Army Recruitment Boards show that there has been an imposing increase in incidence between 1914 and the present day

Peptic ulcer is rare in childhood and adolescence and is most common in early adult life, though it may develop even in old age

In most countries, duodenal ulcer is much commoner than gastric ulcer, while each variety—though especially duodenal—is commoner in men than in women. Thus, in a series of patients attending the Western Infirmary, Glasgow, duodenal ulcer outnumbered gastric by 8 to 1. Among duodenal ulcers there were 4 men to 1 woman, among gastric ulcers 2 men to 1 woman

**Morbid Anatomy** Duodenal ulcers are round or oval. Gastric ulcers, at first round, may spread from the smaller curvature, to assume a saddle shape, and may reach large size. The ulcer is surrounded by smooth mucosa which approaches or overhangs the crater. The excavation has a regular, sharply defined edge, and its walls are vertical,



FIG. 216 Chronic gastric ulcer, situated near the smaller curvature of the stomach and invading the pancreas. Note the fibrosis and in-drawing of the surrounding mucous membrane. (After Cruveilhier)

extending steeply to the floor of the ulcer, so that often there is a typically "punched out" appearance. It is important to recognize that almost invariably there is a complete breach of the muscle coat, no trace of which is recognizable in the floor of the ulcer. The ulcer extends most frequently to the subserous layer, which is fibrous, œdematous and thickened. When the viscus is exposed at operation the only visible indication of the ulcer may be this thickened subserosa, stippled with numerous capillary vessels. In other cases, the external signs of an ulcer are more obvious, the peritoneum is puckered and scarred, œdematous tags of omentum cover it, and there may be adhesion to other organs.

When the ulcer is spreading, small sloughs extend beyond the margins of the crater, satellite acute ulcers appear in the neighbouring mucosa, and, in addition, a varying degree of catarrhal inflammation is present.

Microscopically, the floor and margins of the ulcer show the changes characteristic of a chronic inflammatory process. The crater is lined by necrotic material, and this is surrounded by dense fibrous tissue containing areas of lymphocytic or polymorph infiltration. Often there is



a considerable degree of endarteritis obliterans, and this is of importance in diminishing the tendency to excessive hæmorrhage. Newcomb has drawn attention to another feature characteristic of chronic ulcers, namely, that the muscle fibres at the edge of the ulcer are spread out fanwise and eventually approximate to and fuse with the fibres of the muscularis mucosæ. At the margin of the ulcer the epithelium is distorted by the fibrous tissue and the tubules of the mucosa are dilated and irregular in shape, this is a point of some importance, for the distortion and irregularity may simulate cancer.

### Ætiology of Peptic Ulcer

Since peptic ulcer occurs only in those parts of the alimentary tract to which the gastric juice has access, it is clear that the immediate cause of the ulcer is erosion by peptic digestion. The normal mucous membrane is immune to such digestion. It follows, therefore, that the formation of an ulcer may result either from loss of this protective immunity or from augmentation of the digestive activity of the juice.

It has been suggested that the mucous membrane is devitalized as a result of thrombosis in one of the end arteries of the stomach wall (Virchow) or of infection (Rosenow) but of this there is little evidence. The frequent association of hyperchlorhydria with duodenal ulcer tends to support the view that increase in the digestive activity of the juice is an important factor but it must be recognized that in something like 90% of duodenal ulcers and in the majority of gastric ulcers the acidity is within normal limits.

Recent observations emphasize the importance of a constitutional predisposition to ulcer. A familial tendency is evident in over 10% of cases and is sometimes very striking. Draper has drawn attention to a special anthropometric type which he believes to be associated with the predisposition to ulcer, a type characterized by a particular facial conformation—a long narrow face with deeply etched naso-labial folds—and by certain special features of cranial shape.

Evidence of predisposition is to be found also in the nervous constitution or temperament of ulcer patients, who commonly are of the type described as vagotonic—lean, energetic, restless, over conscientious. This tendency is most marked in cases of duodenal ulcer.

The key to this relationship lies in the innervation of the stomach. Both vagus and sympathetic fibres take part, and while their effects are by no means clear or distinct, it may be said in general terms that the action of the vagus is both motor and secretory while that of the sympathetic is inhibitory. Thus a preponderance of vagus stimulation leads to increased motility with spasm, and to increased secretion with hyperchlorhydria.

It is known moreover that the vagus centre in the hypothalamus is affected markedly by stimulation from the higher centres. In consequence the stomach is very sensitive to psychic and emotional influences. Pavlov's experiments on dogs submitted to sham feeding showed how the mere sight of food stimulated the secretion of gastric juice, while recently Wolf and Wolff by observations on a man with a gastric fistula, have shown that not only the secretion but also the motility

and vascularity of the stomach are influenced by nervous stresses. Indeed, it may be said that the stomach is the mirror of emotions, it may blush with shame or grow pale with rage, writhe in anger or stiffen with fear.

Any theory regarding the ætiology of ulcer must take into account the remarkable increase in frequency during the past fifty years. This clearly cannot be attributed to our constitution or temperament, which remains unchanged through the centuries, but must be due to some alteration in our environment or our reaction to that environment. According to many writers the increase in "wear and tear" of life in this age of rush and hurry is the factor responsible, yet it must be remembered that ulcer is no less common in the Indian coolie than the Wall Street financier. Another factor which has received less attention than it deserves is our dietary which has undergone many fundamental changes during the past half century. McCarrison has provided experimental evidence to suggest that in India a vitamin deficiency is at fault, and it may well be that in Western countries some positive dietetic factor will prove responsible.

The present localization of chronic ulcers to the "ulcer bearing sites" is probably determined by trauma. The lesser curvature and adjacent surfaces of the stomach constitute the principal food route or "magenstrasse" along which passes the great bulk of food entering the stomach, and this area is consequently subject to more than its share of wear or tear. Similarly, the duodenal ulcer bearing areas are situated just where the wall is exposed to the full force of the highly acid chyme expelled through the pylorus.

### Course, Complications and Sequelæ of Ulceration

A remarkable characteristic of chronic ulcers is the periodicity of the clinical features, phases of complete freedom from symptoms alternating with phases of discomfort. It is difficult to believe that the free intervals indicate temporary healing of the ulcer, but rather it would seem that they represent phases of quiescence. True healing of an ulcer of any considerable size can probably not be achieved under the most favourable circumstances in less than several weeks, and if extensive adhesions are present the period required must be longer still.

**Hæmatemesis and Melæna.** The occurrence of bleeding, in the form of a slow ooze from the raw surface, is very common, especially when the ulcer is in an active spreading phase, and the examination of the faeces for occult blood is an important part of the clinical investigation. More copious hæmorrhage occurs less commonly, giving rise to obvious melæna or to hæmatemesis, and may be so severe as to prove fatal. According to Bulmer, more than 10% of cases admitted to hospital on account of hæmatemesis prove fatal.

Hæmorrhage may occur in either acute or chronic ulceration. In Bulmer's 578 cases there were 257 acute and 321 chronic. The more severe types of hæmorrhage are the result of chronic ulceration more often than acute, for the reason that the indurated fibrous tissue at the base of a chronic ulcer tends to prevent retraction of the bleeding vessel. It is important to note, however, that severe and even fatal

hæmorrhage may take place from an ulcer so small as to elude careful search. This is a point of importance when the question of operative treatment is being considered.

Hæmorrhage from an ulcer is occasionally so profuse as to cause death within a few hours. This is most likely to occur when a large vessel, a major branch or even the main stem of one of the arteries supplying the stomach, is eroded. More commonly, however, death occurs as a result of continued or recurrent but less profuse bleeding. The hæmorrhage may not have been copious initially, but is continued or recurs during several days or even a few weeks. In cases of repeated severe hæmatemesis, the mortality rate is over 50% (Davies and Nevin). In such cases, if the bleeding is not too profuse, the red cell count may be maintained at a moderately high level by mobilization of the red cells held in reserve in the bone marrow and spleen, and by rapid production of new red cells. The hæmoglobin, however, cannot be restored so rapidly, and the hæmoglobin content of the blood falls to 20% or even lower. This impairs the transport of oxygen, leads to tissue anoxæmia, and finally brings about a reduction of the alkali reserve (acidosis).

**Acute Perforation.** Acute perforation of a peptic ulcer is now a common complication. It has not always been so. Until the close of the nineteenth century it was rare, but since then its frequency has increased progressively. Thus in Glasgow between 1924 and 1944 the disease has more than doubled in frequency. Moreover there has been a curious change in incidence. In the nineteenth century most perforations were gastric perforations and the majority affected women, especially girls aged from eighteen to twenty-eight years. Now duodenal perforations greatly exceed gastric (in the proportion of nearly seven to one); men are affected far more often than women (again nearly twenty to one); and the curve of age incidence is flatter, with most cases occurring between twenty-five and forty-five years. A perforated gastric ulcer is considerably more dangerous than a perforated duodenal ulcer, for the perforation is generally of larger size and the peritoneal cavity is flooded by large amounts of the highly irritating and sometimes infected gastric contents, whereas a duodenal perforation is usually small and such fluid as escapes is less irritating.

Analysis of a large series of perforated ulcer has brought to light several other interesting features in regard to the incidence of the disease. It has been shown that in Glasgow perforation occurs much less commonly in the months of August, September and October than at other times of the year; it occurs less commonly on Sundays and Mondays than on other days of the week, and it occurs less commonly during the night than during the day. During the day few perforations occur during the morning hours and in the afternoon the frequency gradually increases to a maximum between the hours of 5 p.m. and 6 p.m.

It seems probable that the clue to all these strange cycles of incidence may be found in the healing effect of rest and freedom from strain—the annual holiday, the week-end rest, the night's repose—which transitorily slow down the activity of the ulcer and stave off perforation.

A perforated ulcer may be an acute one of recent onset, but it is far more often chronic, as indicated by the clinical history and the naked-eye character of the ulcer. In about 10% of cases the most careful questioning fails to elicit a previous history of indigestion. In rare cases a patient may suffer two, three or even five perforations, either of the same, or of consecutive ulcers.

Perforation of an ulcer is due to sloughing of an unsupported portion of its floor, probably due in most cases to interference with its blood supply. Often the perforation is of large size, half a centimetre or even larger, rounded or oval and with a smooth, indurated margin. Less frequently the perforation is so small as to be classed as a "leak." Such a leaking ulcer is most commonly situated in the anterior wall of the duodenum. It permits the escape of a little fluid, which gravitates towards the right iliac fossa and may give rise to pain in that area.

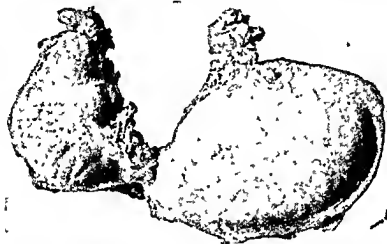


FIG. 217. Hour-glass deformity of the stomach, due to fibrosis round a chronic gastric ulcer.

(Museum of Royal College of Surgeons of Edinburgh)

A leaking ulcer may become occluded by omental adhesion and remain healed, but more often it enlarges gradually and assumes the character of a complete perforation.

The peritonitis resulting from perforation of a peptic ulcer is at first often non-infective, and is due to the irritant action of the gastric or duodenal fluids. The peritoneal exudate may be sterile in nearly 70% of cases (Deaver and Pfeiffer). Owing to reflex inhibition of the secretion of acid gastric juice, however, organisms swallowed in the saliva or already present in the stomach proliferate rapidly, and in the later stages the peritonitis is predominantly infective in type.

**Penetration.** Ulcers on the posterior wall of the stomach or duodenum rarely perforate acutely, but rather tend to penetrate adjacent viscera that have become fixed to the stomach or duodenum by adhesions. The pancreas is the viscus most frequently penetrated, and the ulcer may extend deeply into its substance. In the neighbourhood of the ulcer the pancreas undergoes chronic inflammatory changes, but it is

remarkable that acute pancreatitis is a rare complication, and that there is rarely any demonstrable deficiency of pancreatic function.

In a few cases a posterior ulcer penetrates towards the liver, or it may give rise to abscess formation in the omental bursa or in the subphrenic region. Rarely, a penetrating ulcer may open into the transverse colon, forming a gastrocolic fistula. An ulcer has even been known, in exceptional cases, to perforate into the jejunum, giving rise to a natural gastroyjunostomy.

**Pyloric or Duodenal Stenosis.** This is an end-result of chronic duodenal ulceration, and the stenosis may eventually progress to an extreme degree. Obstruction leads to hypertrophy of the gastric



FIG. 21. Hour-glass deformity of the stomach, in a woman aged forty-three years. The contraction was due to a chronic gastric ulcer.

musculature and to dilatation of the stomach, and this may proceed till the viscus fills the greater part of the abdomen. The dilatation often affects particularly the pyloric antrum, and thus the obstructed stomach is distended to the right as well as to the left of the mid line. In extreme degrees of stenosis there may be almost complete stasis of the gastric contents for twenty-four hours or longer.

When such severe gastric stasis is present, special features may be added. There is great dehydration of the tissues, due to vomiting and loss of fluid into the hugely distended stomach. Later there are headaches, drowsiness and even suppression of urine, so that the condition may be mistaken for the uræmia of late renal disease. Lastly, signs of muscular irritability may develop, culminating in tetanic contractions of the feet and hands—so-called carpo-pedal spasms. These features are now recognized to be manifestations of alkalosis,

which is due partly to the dehydration and partly to loss of hydrochloric acid

**Hour-glass Deformity.** The great majority of examples of this deformity are the results of chronic gastric ulceration, but a few arise

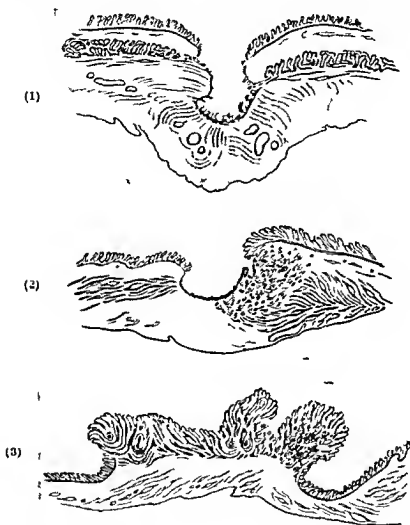


FIG 219 *Ulcer and Cancer of the Stomach* (1) Chronic peptic ulcer The deep crater has penetrated the muscle coat, and its floor is composed of thickened fibrous subserous coat. Note the large blood vessels embedded in fibrous tissue. (2) Ulcer-cancer. Malignant change in a pre-existing peptic ulcer. Epithelium from the mucous membrane at the edge of the crater is proliferating and spreading deeply. (3) Ulcerating cancer of the stomach. The crater is raised above the level of the mucous membrane. Its floor is composed of necrotic tumour tissue.

from malignant disease, or from perigastric adhesions. Exceptionally the deformity is congenital. Women are affected in more than 90% of cases. The contracture usually follows intramural fibrosis around an ulcer. It is usually situated nearer to the pylorus than to the fundus, and consequently the proximal sac is usually the greater. If

the contracture is at a higher point the upper sac may be entirely concealed by the rib margin and may thus be overlooked during operation. The fibrosis has the effect of approximating the greater curvature at the affected point to the smaller curvature, and thus the orifice between the two sacs is never at the lowest point of the upper sac. This is clearly seen in radiograms, in which the opaque meal gives a "water-spout" or "tea pot" appearance. Not infrequently the ulcer heals, leaving a thin fibrous ring encircling the orifice. In other cases an active ulcer may remain, surrounded by a large inflammatory mass and adherent to adjacent structures. Quite commonly the hour-glass deformity is accompanied by pyloric stenosis—hence the lower sac may likewise become greatly dilated.

**Malignant Change in a Chronic Ulcer.** This change, the so-called

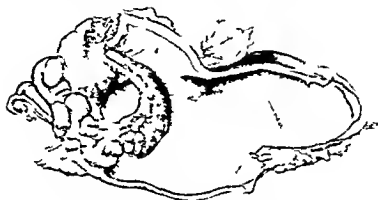


FIG. 220. Ulcer-cancer of the stomach. A large penetrating crater of a chronic ulcer is surrounded by an irregular, raised, indurated carcinoma.

(By courtesy of Mr. J. M. Graham.)

carcinoma *ex ulcere* or ulcer-cancer, may follow gastric ulcer but never duodenal ulcer.

It is important at once to distinguish clearly a carcinoma *ex ulcere* from a primary carcinoma in which secondary ulceration has taken place. The distinction is best made by cutting across the ulcer. A primary peptic ulcer of any considerable size has one very striking feature, namely, that it penetrates the muscular coat of the stomach and erodes a large circular gap in it. A primary carcinoma, on the other hand though it penetrates and invades the muscle, does not destroy it entirely, and traces of muscular fibres may be recognized in its substance to quite a late stage (see Fig. 219).

**Frequency of Malignant Change.** The frequency of malignant change in gastric ulcer is a subject which in recent years has been much debated. It is obviously important from the therapeutic standpoint, for an ulcer that might otherwise be considered suitable for medical treatment cannot justifiably be dealt with medically if it is likely to become malignant, and the same consideration obtains in the choice of conservative as opposed to radical surgical methods.

The estimates formed by different observers of the frequency of ulcer-cancer show wide variations, according to the criteria upon which the diagnosis is based. The problem may be approached from the pathological standpoint, either by examining peptic ulcers for evidence of malignancy or by examining carcinoma for evidence of old ulceration, it may be approached from the clinical standpoint by examining case histories and "follow up" records.

(1) A large proportion of chronic peptic ulcers contain near their margins small groups of atypical epithelial cells arranged in clumps or irregular tubules. Some pathologists have regarded these cells as evidence of early malignancy and have formed a high estimate of the frequency of ulcer cancer. Others, however, look upon such atypical appearances as due to simple hyperplasia or to distortion by fibrosis, and their estimate is correspondingly much lower.

(2) When gastric carcinomata are examined the difficulty is to assess the evidence of pre-existing simple chronic ulcer. According to Newcomb, there are three histological criteria upon which this diagnosis can be based: (a) a complete gap in the muscle tissue of the stomach, (b) old standing fibrosis in the base of the ulcer, (c) approximation or fusion of the muscularis mucosæ and the main muscle layer at the margin of the ulcer. Applying these criteria to 200 specimens of ulcer or carcinoma, Newcomb found six cases in which there was definite evidence of carcinoma originating in a simple ulcer.

(3) On the clinical side, the history of chronic dyspepsia in a case of gastric carcinoma is strong presumptive evidence that the growth has originated in an ulcer. Investigations from this standpoint have, however, given widely varying results.

More reliable figures may be obtained by following up the after history of patients known to have a chronic ulcer. This has been done by Balfour, in cases subjected to the therapeutic test of conservative surgery. In his series of 1,280 cases, mainly treated by simple gastrojejunostomy, less than 6% eventually developed carcinoma of the stomach. Even in these cases, moreover, proof was lacking that the growth originated in the ulcerated portion of the stomach.

Since the observations of competent workers show such wide variations, it is difficult to form an accurate estimate of the frequency of ulcer cancer. It is probably true, however, to say that most authorities believe that not more than 6% of chronic ulcers become malignant, and not more than 10% to 15% of gastric carcinomata arise from chronic ulcers.

### Gastrojejunal and Jejunal Ulcer

Ulcers at or near the stoma constitute a particularly disturbing and troublesome complication of operations for peptic ulcer, and they are largely responsible for the dissatisfaction which, rightly or wrongly, has been felt in recent years in regard to this type of surgery.

Anastomotic ulcers occur nearly always in males, and as a complication of operations for duodenal ulcer. They are rare following operations for gastric ulcer, and almost unknown in cases of gastric carcinoma.



The frequency of anastomotic ulceration has been the subject of much controversy. It has been variously estimated as occurring after 1% or as many as 15% of gastric operations. The most reliable statistics are those of Walton who followed up every one of 1809 gastric and duodenal cases operated upon by himself. In this series gastrojejunal ulcer developed thirty times an incidence of 1.6%. In twenty nine cases the primary operation was for duodenal ulcer in the remaining case it was for gastric ulcer.

The type of primary operation most likely to be followed by ulceration at the anastomosis is gastrojejunostomy, but gastrectomy and the various types of gastroduodenostomy are not immune. In Walton's

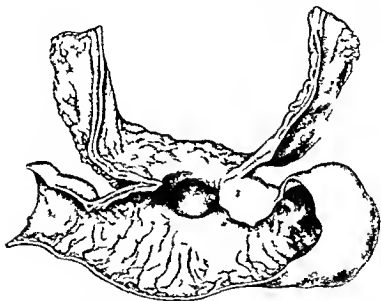


FIG 401 Gastro-jejunal ulcer. A deep ulcer is seen immediately on the jejunal side of the anastomosis. Death resulted from hæmorrhage from an artery which can be seen at the right side of the crater.

(By courtesy of Prof J W S Blacklock.)

series gastrojejunal ulcer occurred in 3.2% of the cases subjected to gastrojejunostomy and in 0.43% of those subjected to partial gastrectomy. It is generally thought that anterior gastrojejunostomy is more liable to this complication than the posterior operation although this view is not borne out by Walton's investigation.

Secondary ulceration is most likely to arise in the presence of that most important factor, an increased acidity of the gastric juice. The importance of this is demonstrated by the fact that in spite of the added neutralization afforded by the anastomosis 70% of cases of gastrojejunal ulcer show persistent hyperchlorhydria. For this reason a patient with much hyperchlorhydria being particularly liable to secondary ulceration should not be submitted to gastrojejunostomy.

There is some evidence to suggest that the hyperchlorhydria is a congenital, and perhaps a familial disorder. It is noteworthy that some patients are particularly prone to develop anastomotic ulcers, whatever the type of operation performed. They may develop new ulcers successively after repeated operative interference.

Formerly it was usual to attribute an important rôle in the formation of anastomotic ulcers to local agents resulting directly from the operative procedure, e.g., torsion or other malposition of the jejunal loop, clamp trauma, the occurrence of a hæmatoma at the suture line, or the irritation of an unabsorbable silk thread. Some of these possibly play a part in a few cases, but their importance is undoubtedly much less than was at one time thought. Other predisposing factors include those which have been mentioned in connexion with the ætiology of peptic ulcer in general, namely, infective foci, tobacco, highly acid foods, irritant foods and irregular meals.

Gastrojejunal or jejunal ulcers may occur at almost any period after operation, from a few weeks to several years. In a large proportion of patients in whom this complication develops it is possible to obtain a history of pain in the immediate post-operative period, and it seems likely that the great majority of ulcers originate then—a point which emphasizes the need for careful post-operative diet and alkali treatment. Ulcers that first give rise to symptoms later than four years after operation are uncommon, although there are cases on record in which the symptoms appeared as late as fourteen years after the original operation.

The ulcer may be situated either near the anastomosis, at its margins or in the jejunum at some distance from the opening. The majority abut on the line of anastomosis, either on its gastric or jejunal side and the suture line forms one margin to the ulcer. According to Walton, jejunal ulcers remote from the anastomosis are exceptional. When they occur they are situated in the jejunum directly opposite, or a few centimetres down the efferent loop, but very seldom in the afferent loop, owing to the alkalinity of its contents. In its life history the ulcer resembles a chronic gastric or duodenal ulcer, and is equally apt to bleed and to perforate into the general peritoneal cavity. It possesses a somewhat distinctive feature, however, in a special tendency to adhere to neighbouring structures, especially the mesocolon, and to form a large inflammatory mass round a relatively small crater. The ulcer is moreover apt to implicate adjacent viscera, particularly the colon, and eventually to perforate into it, with the formation of a fistula. The fistula may be between the stomach and the colon—*gastro-colic fistula*, between the anastomosis and the colon—*gastro-jejunocolic fistula*, or between the jejunum and the colon—*jejuno-colic fistula*. The development of a fistulous communication by permitting reflux of colon contents into the jejunum gives rise to enteritis, with diarrhoea, dehydration, and in some cases severe malnutrition. Reflux of colon contents into the stomach may lead to foul eructations and fecal vomiting. It is noteworthy that when the fistula is well established pain may be lessened or disappear as there is a tendency for the ulcer to heal.

## Pathological Complications of Operations for Ulcer

The operation of gastrojejunostomy, so uniformly successful for the relief of severe pyloric stenosis was by contrast liable to a variety of complications when performed in cases of peptic ulcer without stenosis. Some of these complications supervened early after operation, and were then usually due to technical errors in its performance. They included obstruction at the anastomosis due to such various causes as torsion or angulation of the jejunum, herniation of small intestine behind the anastomosis or through the opening in the transverse mesocolon and retrograde intussusception of small intestine through the stoma into the stomach.

Other complications of gastrojejunostomy occur at a later stage after the operation. Of these, by far the most important was stomal or jejunal or anastomotic ulcer, with its sequel gastrojejunocolic fistula. They have already been discussed (*see p. 469*).

*Partial Gastrectomy* is also liable to complications and its use as a routine method of treatment for peptic ulcer is as yet too recent to compare their frequency with those following the older operation of gastrojejunostomy.

Leakage from the duodenal stump is one of the most dangerous of the early complications. The duodenum is thin walled only partly enclosed in peritoneum and commonly fixed by dense scarring to the head of the pancreas and other neighbouring tissues and in consequence its secure closure by sutures may be technically difficult. Probably also distension of the duodenum due to temporary hold up in the proximal jejunum by spasm or oedema at the stoma predisposes to leakage at the duodenal stump. Once the leakage has occurred, the enzyme activity of the copious duodenal juices maintains the leakage and prevents natural closure. In some such cases the free chemical peritonitis which results quickly brings about a fatal issue; in others the leaking content finds its way to the surface and leads to the establishment of a duodenal fistula with its attendant complications of dehydration, demineralization and skin digestion.

The *post prandial syndrome* is a not infrequent complication of gastrectomy particularly when performed for duodenal ulcer. It appears within a few weeks after the operation and may persist for several months. The symptoms develop a short time after meals—sometimes during the meal—and are characterized by nausea, epigastric distension, sweating and a feeling of great weakness necessitating recumbency. In severe cases the symptoms persist for an hour or so and then terminate abruptly after the vomiting of a considerable quantity of bile.

This post prandial syndrome has been attributed to hypoglycæmia. In some respects indeed it does resemble hypoglycæmic attacks induced for example by an overdose of insulin. Moreover, it is established that after gastrectomy owing to rapid passage of carbohydrate foods into the absorption area of the jejunum there commonly occurs a rapid rise in the blood sugar followed by a steep fall to a level below normal. Two pieces of evidence however appear to show that hypoglycæmia is

not the true explanation of the post prandial syndrome. Firstly, if the blood sugar is estimated at frequent intervals after a meal, it is clear that the symptoms commonly develop before the hypoglycæmic phase, indeed they commonly develop before the hyperglycæmic phase and often are terminated before the blood sugar has fallen to below the normal level. Secondly, the symptoms bear no relation to the carbohydrate content of the meal, they may occur after a meal rich in protein or fat and may fail to occur after ingestion of pure sugar.

Generally the bulk of the meal is of more significance than its composition. This indicates that the syndrome is of reflex character, due perhaps to distension of the small remaining pouch of stomach, or perhaps to "dumping" in the jejunum. In some cases it may be due to obstruction to, and dilatation of the duodenum as the over filled stomach displaces and compresses the afferent opening of the stomach. This is suggested by the common experience that relief from the symptoms coincides with the vomiting of a large amount of bile, which presumably has just been released from the obstructed duodenum.

## CARCINOMA OF THE STOMACH

This is one of the commonest of new growths in man, and from its malignancy, its insidiousness of onset, and its deep seated situation, it is one of the most difficult to eradicate. It occurs most commonly between the ages of forty and sixty, though occasionally it may be found much earlier in life. The male sex is affected more often than the female, in the proportion of 3 to 2.

It is generally believed that there are two important predisposing factors—chronic gastritis and gastric ulcer. The views held in regard to the relationship of gastric ulcer to carcinoma have already been discussed, and it will be sufficient to state here that such a relation can only be demonstrated in a small proportion, perhaps 10% to 15% of cancers.

Chronic gastritis has often been regarded as an important predisposing factor. To some extent this view may have been fostered by confusion of "chronic gastritis" with "chronic gastric ulcer," terms which formerly, and particularly in continental papers, were often regarded as synonymous. Apart from ulcer, there is little or no evidence that gastritis predisposes to cancer.

The relation of achlorhydria to gastric carcinoma has been clarified by recent work. Often acid is present in normal amount—even, occasionally, in excess, in the early stages of cancer, and the subsequent development of achlorhydria is clearly a consequence of the malignant disease or the secondary infection to which it gives rise. A number of cases have been reported, however, of cancer developing in persons known for many years to have achylia, and it may well be that such a sequence occurs more often than hitherto suspected.

There are some interesting differences between the incidence of carcinoma of the stomach in different countries. In Great Britain, carcinoma of the stomach accounts for 22% of all types of cancer in

man, as compared with 42% in America, 55% in Holland, Bavaria and Spain, and 66% in Czechoslovakia. According to Hurst, the differences in this country and Holland are mainly accountable by dietetic habits, for work done under his supervision appears to show that the Dutch smoke more, consume more alcohol and spiced and overheated foods, chew their food insufficiently and eat it too quickly. Oral sepsis, which is also more common in Holland than in this country, may be another predisposing factor.

It is usual to describe four principal varieties of gastric cancer: (1) the sessile or ulcerating, (2) the polypoid or proliferative, (3) the colloid or mucoid, and (4) the atrophic or leather bottle. The fourth



FIG. 222. Carcinoma of the stomach (seen from behind). The growth has originated near the pylorus and has spread thence, encircling and constricting the pyloric antrum.

(Department of Surgery, University of Edinburgh.)

variety, though rare, is such a distinctive one as to be regarded separately, but it should be clearly recognized that the others are not so much distinct diseases as deviations from a common type. The great majority of gastric carcinomata are intermediate forms having some of the characteristics of all. A fifth type of growth requires also to be mentioned, a squamous-cell carcinoma which is occasionally found at the cardiac end, it may be derived from the lower end of the œsophagus or from heterotopic œsophageal mucous membrane in the stomach close to the cardia.

(1) **The Sessile or Ulcerating Form.** This is the most common type of growth, and is also the most malignant for it is usually symptomless in the early stages, it infiltrates widely, and soon gives rise to metastases. It occurs principally in the pyloric region and at the smaller curvature,

though no part of the stomach is exempt. The growth is of a scirrhous nature, hard and fibrous. At first it is confined mainly to the mucous and submucous coats, extending widely in these planes, later it penetrates the muscularis to reach the peritoneal aspect. The surface of the growth is usually ulcerated, with a shallow crater lined by necrotic malignant tissue and with hard, raised, rolled margins.

Microscopically, growths of this type are composed of spheroidal or sometimes columnar epithelial cells in a well formed fibrous stroma. The epithelial cells may be arranged in irregular tubules or acini but are often scattered irregularly in small groups. To this latter type the term "carcinoma simplex" has sometimes been applied.

(2) **The Polypoid or Proliferative Form** This is a less common type

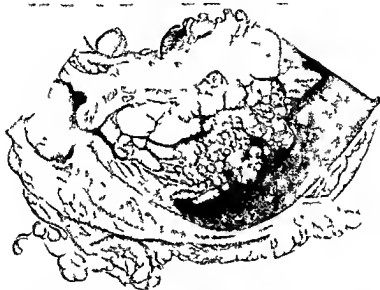


FIG. 223. Carcinoma of the stomach. The growth which has originated near the smaller curvature forms a massive tumour projecting into the cavity of the stomach. Note the hypertrophy and fragmentation of the muscle coat.

(By courtesy of Mr J. M. Graham.)

It forms a bulky, soft, cauliflower like mass which projects into the stomach. When situated towards the pylorus it tends, in virtue of its bulk, to cause obstruction. The superficial part of the growth rapidly degenerates and local surface ulceration occurs leading to hemorrhage, secondary infection and to cachexia.

Microscopically, this type of growth is usually composed mainly of columnar cells, arranged principally as irregular tubules or acini, but spheroidal cells also are found. The tumour is often soft or "encephaloid," with a scanty, poorly formed stroma, and degenerative changes are common.

(3) **The Colloid or Mucoid Form** This variety also occurs as a rule in the pyloric region. It is somewhat rare, and is usually regarded as a form of degenerative change rather than a special type, but its characteristics are sufficiently distinctive to merit separate description. The

tumour on section has a peculiar translucent appearance. A characteristic feature is the tendency of the growth to extend to the peritoneal surface. Adjacent structures are invaded, and the liver, spleen and other organs may be glued together by a thick casing of gelatinous material. Microscopically, the striking feature is the large amount of mucoid material, which is situated both inside the malignant cells and in the stroma. Large globules fill the cell protoplasm and displace the nucleus to one side, giving an appearance comparable to a signet ring. The same appearance is present in metastases.

(4) *The Atrophic or Leather-bottle Form.* This is a slow growing carcinoma which spreads entirely in the wall of the stomach, only invading lymph glands and distant structures at a very late stage. It



FIG 224 Cancer of the stomach. The tumour is composed of spheroidal and columnar cells in an irregular acinar formation.

(Department of Surgery, University of Edinburgh.)

is characterized by the presence of much fibrous tissue. Beginning usually in the pyloric region, it extends proximally and may eventually implicate the whole stomach from the pylorus to the cardia (see Fig 225). In an extreme case, the stomach is greatly contracted and its capacity may be reduced from the average normal content of one to two pints to a few ounces. The wall is diffusely indurated, sometimes measuring 2 cm. or more in thickness, and on its serous aspect it is pale and almost pearly white. The mucous membrane is rugose, and is often oedematous, congested and altered by secondary catarrhal changes. In a considerable proportion of cases there is an ulcerated area, often in the pyloric region, and it is usually presumed that this indicates the site of origin. On cross section it is seen that the thickening affects principally the submucous and subserous coats, which are infiltrated with dense fibrous tissue. The muscular coat presents a striking appearance, for the circular coat is greatly hypertrophied, and its fibres are, in addition,

traversed by dense white bands connecting the submucous and subserous layers, an appearance often described as segmentation of the muscle. Although such great contraction and thickening of the wall is present, there is no stasis, but on the contrary food passes into the duodenum with great rapidity.

Microscopic examination shows that the cancer cells are scanty, and buried in fibrous tissue, so that examination of several sections may be necessary before the malignant nature of the condition can be deter-

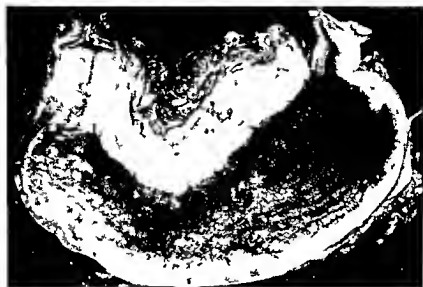


FIG 225 Leather bottle carcinoma of the stomach. The stomach is of small size and the whole of its wall is infiltrated and greatly thickened. The mucous membrane is oedematous and being redundant it is thrown into folds.

(Department of Surgery University of Edinburgh)

mined. The cells are spheroidal, and are scattered through the tissues in small clumps rather than arranged in definite masses or alveoli.

At a late stage of the disease metastases occur in the regional lymph glands as well as in the liver and more distant situations, but for a long time the carcinoma remains limited to the stomach. If technical considerations warrant the operation, complete excision is indicated.

### Spread of Gastric Carcinoma

In any of the types just described the disease spreads at first and principally by the lymph channels within the stomach wall, but in most cases, except in the "atrophic" form, at a relatively early period it reaches neighbouring lymph glands. Later, the adjacent viscera and tissues are invaded by direct extension, and dissemination may take place through the peritoneal cavity and by the blood stream.

(1) *In the Stomach Wall* This early spread, most obvious in the infiltrating or leather bottle type, is nevertheless extensive and important in the other forms and in particular in the scirrhus, ulcerating type. The submucous layer may be infiltrated with pale-white streaks



of malignant growth far beyond the limits of the actual ulcer, and around this visible zone is an even more extensive microscopic spread.

When the tumour is situated on the smaller curvature, the submucous extension is chiefly in the direction of the cardia, and around the anterior and posterior surfaces. Sometimes the cardiac orifice is involved, and secondary oesophageal obstruction results. The growth rarely encroaches upon the pyloric ring, and the duodenum is only likely to be invaded from a secondary nodule implanted on its serous surface.

(2) *To Lymph Glands.* Metastases in lymph glands frequently appear at a very early stage of the disease. The first to be affected are



FIG. 226. Infiltrating carcinoma of the stomach. A radiogram after the administration of barium. The stomach is greatly reduced in size and narrowed by the infiltrative growth.

usually the glands nearest the tumour and, from the usual situation of the tumour on the smaller curvature near the pylorus, two groups in particular are liable to early involvement. These are (a) the lower coronary group, situated between the layers of the small omentum close to the distal part of the smaller curvature, and (b) the pyloric and subpyloric group, which are placed close to the first part of the duodenum and in the angle between it and the head of the pancreas.

From the lower coronary group the growth tends to spread to the upper coronary group (rarely these may be the first to be involved) and thence to glands along the coeliac artery and to the para aortic chain. The growth may extend in retrograde manner from the coeliac

artery to reach the lymph glands in the porta hepatis, whence the liver may be affected

From the pyloric and subpyloric glands the disease may extend to the supra pancreatic glands and glands at the root of the mesentery. A malignant mass in the last situation may compress the third part of the duodenum and lead to duodenal obstruction

If the primary growth lies near the greater curvature it tends to spread to lymph glands of the gastro epiploic chain, between the layers of the gastrocolic ligament and in the great omentum. Such spread is less important, however, for these glands in turn drain back into those of the subpyloric group

(3) *To Adjacent Organs* The primary growth may extend directly into the pancreas, omentum or liver. Less commonly, there is invasion of the spleen and the colon and occasionally of the jejunum

(4) *By the Peritoneal Cavity* When the growth has extended to the serous surface of the stomach, malignant cells are liable to be set free and to traverse the peritoneal cavity. Here they may give rise to numerous widely scattered metastases, at first small like tubercles, and later growing extensively, or they may result in one or more large masses. These massive peritoneal metastases are particularly apt to arise in the great omentum, on the pelvic floor, or on the surface of one or both ovaries. In any of these situations a large secondary mass is liable to be regarded as a primary growth, particularly as the primary growth in the stomach may be almost symptomless

(5) *By the Blood Stream* This usually occurs at a late stage of the disease, but in young subjects may take place early. The liver is affected first, later, metastases are found in the lungs, brain, bones and other viscera

## SARCOMA OF THE STOMACH

Sarcoma may arise in any of the connective tissues of the stomach wall. It is of rare occurrence constituting about 1% of all gastric tumours. It may develop at any time of life, but generally at an earlier age than carcinoma. The average age is about forty

The tumour differs in no essential respect from a sarcoma elsewhere. It forms a large mass, which undergoes central necrosis early, and forms an extensive ulcer from which free hæmorrhage may occur. Secondary infection leads to rapid cachexia and death. The commonest form is a lymphosarcoma arising in the lymphoid tissue of the submucous coat. Sarcoma sometimes arises in a leiomyoma. Round cell and spindle cell sarcoma also are described

The tumour is situated most often in the pyloric antrum, but is rarely so close to the pylorus as to cause early stenosis. Achlorhydria is usually present, but this is by no means invariable. It is a remarkable fact that occasionally there is little loss of weight until the late stages of the disease

Atypical forms of *lymphadenoma* (Hodgkin's disease) occasionally give rise to infiltration and extensive ulceration of the stomach and thus may progress in much the same way as sarcoma

**SIMPLE TUMOURS OF THE STOMACH**

**Gastric Polyposis** Polypoidal projections of the gastric mucous membrane are common near the margins of a gastric carcinoma, but the term gastric polyposis is restricted to a comparatively rare condition of simple papillomatous overgrowth. The polypi are papillary adenomata which arise in the mucous membrane and project into the cavity of the stomach. They are usually multiple, but single polypi have been reported. A rare form of polypus is that in which a limited area of the gastric mucosa is affected in a diffuse fashion, being raised in a well defined velvety plaque in an otherwise healthy stomach.

At operation a group of polypi may be felt inside the stomach as a soft doughy or worm like mass. The mucosa is covered with velvety red projecting masses, which vary in size up to that of a cherry, and are widely distributed, either in the pyloric portion or through the whole stomach. Ulceration and secondary infective changes are common, and often there is some catarrhal gastritis. Microscopically, the tumours are papillary adenomata, composed of columnar cells arranged in well formed acini and supported by a lax connective tissue stroma. In the diffuse plaque like variety the tubules of the growth resemble the duodenal glands of Brünner. Gastric polyposis is very liable to be mistaken for carcinoma, the ulcerated surfaces bleed readily and a severe degree of secondary anæmia sets in, catarrhal changes reduce the gastric acidity, perhaps to zero, the vomit contains blood, mucus and even lactic acid, and on radioscopic examination the barium shadow is interrupted by numerous filling defects. In many of the reported cases carcinoma has supervened, but there does not appear to be that intimate relation between the two conditions which is found in the colon.

Other simple tumours of the stomach are rare. A myoma occasionally is found. It may project into the lumen or subperitoneally, and in either event forms a smooth rounded or nodular lump, often of considerable size, and often pedunculated. Cases have been reported in which such a tumour has caused symptoms from pressure. When it projects towards the lumen the tumour may ulcerate and simulate a malignant neoplasm, or it may be propelled towards the pylorus and cause obstruction at that point, or even intussusception. Rarely the presence of a large tumour has led to volvulus of the stomach.

Fibroma, lipoma, and angioma of the stomach may occur.

**SYPHILIS OF THE STOMACH**

Syphilitic affections of the stomach are uncommon, and of interest chiefly from their mimicry of carcinoma. They occur as late tertiary manifestations of the disease and begin as a gummatous infiltration of the submucosa, usually on the smaller curvature towards the pylorus.

The disease may progress to the formation of single or multiple gummatous ulcers or submucous nodules, or it may lead to extensive fibrosis of the affected part of the stomach wall.

In some cases a large gumma forms, softens in the centre and breaks down, giving rise to a large ulcerating mass resembling an ulcerating carcinoma. More commonly, syphilis leads to diffuse fibrosis of the stomach wall. If this occurs in the region of the pylorus, pyloric stenosis is the natural result, if in the body of the stomach an hour glass deformity. Rarely syphilitic fibrosis affects the greater part, or even the whole of the stomach, and gives rise to a condition readily mistaken for "leather bottle" carcinoma or for fibromatosis of the stomach.

The effects of syphilis of the stomach may resemble those of gastric ulcer or carcinoma. Hæmorrhage from the ulcerated surface, manifest in hæmatemesis or melenæ, leads to severe anemia. Secondary catarrhal gastritis leads to excessive production of mucus and in 85% of cases to complete achlorhydria. The diagnosis is rendered difficult by the fact that the disease often fails to respond to ordinary anti-syphilitic measures.

### TUBERCULOSIS OF THE STOMACH

Tuberculous affections of the stomach and duodenum are extremely rare, a remarkable fact considering that the tubercle bacillus can survive exposure to gastric juice for several hours, and considering that infection of the lower alimentary tract from swallowed sputum is so common.

The most frequent tuberculous lesion is a single ulcer on the smaller curvature towards the pylorus, it has the characteristics of a tuberculous ulcer elsewhere, and has no distinctive clinical features. Occasionally several small milary ulcers are present. Rarely a hyperplastic type of the disease occurs, with much fibrosis and little or no caseation, this variety at the pylorus may lead to stenosis and as at the ileocecal region, it may simulate carcinoma.

Tuberculous disease in the stomach is generally believed to follow infection from swallowed sputum, rarely a caseous lymph gland may adhere to the stomach wall and thus infect it.

### CONGENITAL HYPERTROPHIC PYLORIC STENOSIS

A disease of the early weeks of life, affecting boys four times more frequently than girls, and especially prone to attack the first born of the family. The muscular wall of the pyloric canal is hypertrophied, and this leads to narrowing of the lumen and obstruction. Distally, the hypertrophy is clearly delimited, for it never goes beyond the pylorus. Proximally, the limitation is less exact and the hypertrophy gradually diminishes until at the incisura angularis the muscle is of normal thickness. At the pyloric canal the swollen muscular wall forms a rounded bobbin like mass. The circular muscle is particularly affected and its fibres are pale compared to those of normal muscle, grey or greyish white and poorly supplied with blood. Partly owing to the muscular overgrowth and partly owing to redundancy of the mucous membrane which becomes folded upon itself, the lumen of the pylorus is greatly reduced. The stomach and even the œsophagus, hyper-

trophies in efforts to overcome the obstruction and causes vigorous peristalsis, as is readily seen if the infant is examined during a feed. Later the stomach dilates and its mucosa undergoes secondary catarrhal changes.

Congenital pyloric stenosis is an inherited abnormality of recessive type, while sex and primogeniture are also determining factors. The underlying cause is the possession of a pair of abnormal genes, one from each parent, and should the recipient chance to be a boy and first born, his chance of being affected is the Mendelian ratio 1 in 4. Girls and subsequent children are much less likely to be affected.

There have been numerous theories as to the significance of the pyloric lesion. Hirschsprung and Cautley maintained that the primary

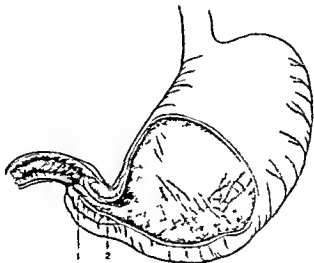


FIG. 22. Congenital hypertrophic pyloric stenosis from a male aged five weeks. Note (1) the great hypertrophy of the circular muscle fibres (2) the fold of redundant mucous membrane. The stomach is greatly dilated.

lesion is a congenital muscle hypertrophy, and that the pyloric obstruction is due to the increased thickness of the muscle and to the resulting spasm. John Thomson, on the other hand, suggested that the primary factor is a want of neuro-muscular coordination, which leads to functional obstruction at the pylorus and to compensatory hypertrophy of the muscle fibres of the pyloric canal.

The clinical features are characteristic. The first sign usually appears within a few days or weeks of birth, when the baby, previously healthy, commences to vomit, the vomiting becomes forcible and projectile, from extreme muscular activity, and tends to occur within a few minutes of the beginning of a feed. The onset thus differs from that of congenital intestinal atresia, which is manifest from birth, and the vomit differs from that of volvulus of the mid gut loop (*see p. 491*) in containing no bile.

There is another rare form of pyloric stenosis in children, due to a congenital defect—the stenosis of Landerer and Maier. The obstruction in this case is due to a diaphragm of mucous membrane at the pylorus, pierced by a very small hole. The symptoms in this type do not begin until later childhood.

### VOLVULUS OF THE STOMACH

This rare accident may involve the whole stomach, or its pyloric portion alone. The partial variety generally occurs as a complication of hour glass deformity, for in this condition the lower pouch, slung between the contracture and the pylorus, is relatively free to rotate. The complete variety is most likely to occur in association with diaphragmatic hernia, a benign gastric tumour, or of perigastric adhesions. In some cases the only predisposing factor is gastropptosis.

The volvulus may take place round an axis passing through the two orifices of the stomach, or one perpendicular to this line. In the former, organo axial type, the greater curvature generally passes forwards and upwards, and comes to lie under the anterior part of the diaphragm. The transverse colon may be drawn upwards with the greater curvature and become impacted under the diaphragm. In the latter, mesenterio axial type, the pyloric part of the stomach passes forwards, upwards and towards the left in front of the body of the stomach, carrying the right colic flexure with it. In this type the volvulus is generally of limited extent.

The main effect of volvulus of the stomach is to cause complete obstruction of the pylorus, and in some cases of the œsophageal orifice. There is little interference with the blood supply to the stomach. The stomach becomes greatly distended, causing severe epigastric pain and extreme collapse. Large quantities of fluid are lost into the dilated viscus, and dehydration is consequently a marked feature. If the œsophageal orifice is obstructed there is no vomiting, and attempts to pass a stomach tube are unsuccessful. In some cases secondary obstruction of the colon is a complicating feature.

### ACUTE DILATATION OF THE STOMACH

This is a remarkable condition in which for no obvious reason the stomach becomes rapidly ballooned with gas, so that it fills the greater part of the abdominal cavity. Generally it is a post operative complication, but it may follow simple manipulations, such as the application of a plaster case, and rare cases have been recorded in which it arose from no obvious cause in otherwise healthy young adults. The predisposing operation is most commonly an abdominal one, performed for affections of the female pelvic organs, the appendix, or gall bladder. It is curious that operations on the stomach itself practically never predispose to it. There appears to be no relation between acute gastric dilatation and infections.

Acute post-operative dilatation of the stomach rarely becomes manifest later than forty eight hours after operation; sometimes it occurs within a few hours, and in a few recorded instances it has occurred

actually during the operation. These cases are of particular interest, the stomach is suddenly observed to be increasing in size, and within a few minutes it fills the greater part of the abdomen and projects at the wound, after passage of a stomach tube a quantity of gas, of the composition of atmospheric air, is released, and the stomach immediately returns to its normal size.

The stomach may reach to the brim of the pelvis, its wall becomes greatly thinned, the mucosa eroded; and the gas later becomes replaced by foul, blood-stained fluid. The dilatation may be limited to the stomach, but this is unusual, and it commonly extends to some point in the second or third parts of the duodenum or even to the proximal coils of the jejunum. In about a quarter of the recorded cases the dilatation stopped short at the point where the duodenum is crossed by the superior mesenteric vessels (gastro-mesenteric ileus).

The cause is not fully understood. It is, however, generally agreed that the stomach is affected first and principally, and that duodenal dilatation, when present, is a secondary phenomenon, due to compression of the root of the mesentery from the drag of displaced small intestine. A healthy stomach when distended empties itself by the forcible expulsion of gas along the œsophagus, and it must therefore be presumed that before dilatation can occur there must be paralysis of the gastric musculature, and possibly also spasmodic contraction at the cardia, these predisposing affections may possibly arise from toxic changes in the muscle, but their sudden onset suggests rather a reflex action. The gas which fills the stomach might be thought to arise from the fermentation of intestinal contents, but this could hardly explain the extreme rapidity of the dilatation. McIlvor has shown that in the cat some degree of gastric dilatation may be brought about by inserting a valvular tube into the upper part of the œsophagus, allowing air to be sucked down into the stomach but preventing its exit and it is possible that some valvular mechanism may occur in man.

The effects of acute dilatation are immediate, grave, and sometimes fatal. In part, they arise from the mere distension of the stomach, which displaces other viscera, pushes up the diaphragm and interferes with the action of the heart. Even more important, however, is the subsequent outpouring of fluid into the dilated viscus, for the tissues become dehydrated, the secretion of urine diminished, and alkalosis rapidly develops. If the duodenum is obstructed the effects of a high intestinal obstruction are superadded. It is not surprising that there is rapid collapse and great dehydration, at first there may be no vomiting, but later an overflow regurgitation may occur. Fortunately if recognized early the condition is amenable to treatment by passage of the stomach tube.

### CHRONIC DUODENAL ILEUS

Chronic obstruction of the duodenum may arise from one of several causes which fall naturally into two principal groups. The first is that in which some gross obstructing lesion is demonstrable, for

instance, calcified tuberculous lymph glands, or infiltration of the mesentery by malignant disease, or rarely, adventitious adhesions in this region. The second includes those in which there is no definite organic disease to account for the obstruction.

The second group occurs most often in females and usually in those of visceroptotic habitus, but it may rarely be found in those of sthenic build. Obstruction is situated usually at the point of crossing of the superior mesenteric artery, and it is generally attributed to the pull of these vessels associated with a greater or less degree of prolapse of the small intestine (arterio mesenteric ileus). In some cases it appears as though displacement of the small intestine and consequent

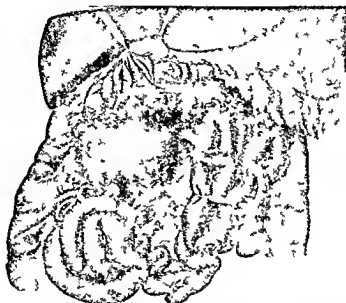


FIG. 298. Chronic duodenal ileus. The transverse colon has been drawn up and the peritoneum incised to show the third part of the duodenum which is greatly distended. The root of the mesentery containing the superior mesenteric vessels is seen immediately to the medial side of the distended duodenum.

mesenteric traction is due to primary dilatation of the stomach or to gastropptosis. Rarely the obstruction appears to result from traction by the proximal colon upon the right colic artery, which crosses the third part of the duodenum obliquely. Very often it is not possible to demonstrate any obstruction, and the dilatation is merely part of a general visceroptosis. Anatomical observations indicate that at birth there is often a slight constriction of the duodenum where it is crossed by the mesentery, and it is possible that some such developmental narrowing predisposes to the condition, but although occasionally seen in childhood duodenal ileus usually becomes manifest only in adult life.

The third part of the duodenum is generally the most affected, and it may so dilate as to bulge forwards below the transverse mesocolon. Occasionally the dilatation is most obvious in the first and second parts of the duodenum which project like a second stomach to the right of



the pylorus. The stomach is always large also, but the pylorus may or may not be dilated.

Duodenal ileus is important in itself, as a possible cause of severe bilious attacks, but it is equally important in that it may prejudice the success of operation on other parts of the abdomen. It is no doubt responsible for some instances of pernicious vomiting after gastro-jejunostomy, and it may be responsible for leakage from the duodenal stump after gastrectomy.

## DUODENAL DIVERTICULA

Duodenal diverticula are usually regarded as somewhat rare lesions, but according to several anatomical studies it would appear that they are not uncommon. Failure to recognize them is due to the absence of any definite symptomatology, and to the difficulty of portraying them by radiography. Apart from a rare form of pouching which occurs exactly at the duodenal papilla, two types of diverticula may be recognized—the primary type, in which no obvious cause can be discovered, and the secondary type, which results from some local lesion.

*Primary diverticula* occur usually in the second part of the duodenum, rarely in the third and fourth parts, and never in the first part. They form flask like protrusions from the concave border of the gut, and are closely related to the vessels entering the duodenal wall. The diverticula are often multiple, and reach their greatest development in middle-aged or old persons. Microscopically, they are found to be composed of the mucous and submucous coats, which have herniated through a gap in the muscularis. The pouches are closely related to the pancreas, and occasionally small islands of aberrant pancreatic tissue are embedded in their walls. They may exert injurious pressure on the common bile duct and the pancreatic duct.

They are usually symptomless and only discovered by chance in the course of radiographic examination of the digestive tract, in some cases, however, vague symptoms of indigestion have been attributed to them. It is remarkable that infection and other complications only supervene with great rarity, owing, no doubt, to the relative sterility of the duodenal contents. In exceptional cases, stasis in a pouch has predisposed to the formation of concretions.

*Secondary diverticula* are commonest in relation to peptic ulcer, and consequently occur in the first part of the duodenum. They may arise from the direct traction of an ulcer cicatrix, or from the stretching and "pulsion" of a weakened area of the wall. In either case, they have little clinical import and have no symptomatology apart from that of the causative lesion.

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## CHAPTER XXIV

### DISEASES OF THE SMALL INTESTINE

#### ANOMALIES OF INTESTINAL ROTATION

The mid-gut which includes the small and large intestine from the level of the duodenal papilla to the neighbourhood of the left colic flexure undergoes a complicated series of rotations in early foetal life. An understanding of the mechanism of this evolution, and of the derangements to which it is subject, is of considerable importance to the surgeon, for anomalies of rotation may result in errors in the location of the duodenum the appendix or the caecum which confound the unwary operator, or they may give rise to secondary pathological changes which it is important to understand.

**Mechanism of Normal Rotation.** The mechanism of normal rotation has been investigated by several embryologists, and Dott has given an excellent account of it, with, in addition, a valuable description of the various anomalies and their clinical significance. The most complicated evolutions take place before and during the tenth week of intra-uterine life and before proceeding to describe them it will be necessary to consider the state of the intestinal tract at their inception.

The gastro-intestinal tract consists of three portions, the fore-, mid-, and hind-gut, of these, the fore-gut includes the stomach and the duodenum as far as its papilla, the mid-gut includes from the duodenal papilla to the region of the left colic flexure, and the hind gut includes the distal colon. In early intra-uterine life each of the three portions is suspended from the dorsal wall of the body cavity by a mesentery, which contains the blood vessel to the three loops, respectively, the coeliac the superior mesenteric and the inferior mesenteric artery.

The mid-gut at this time consists of a single short loop supported by a somewhat fan-shaped mesentery attached to the dorsal wall of the body cavity by a narrow pedicle the "duodenocolic isthmus." This isthmus is bounded above and below by the two extremities of the mid-gut (the duodenum and left colic flexure) and these two points lie closely opposed to each other in the mid line (*see Fig. 229*). Passing ventrally at the isthmus between the two layers of the mid-gut mesentery is the superior mesenteric artery and in its course towards the convexity of the loop it gives off branches to all parts of the mid-gut. The proximal or pre-arterial branches become the vasa intestinales and the portion of gut they supply becomes the jejunum and ileum, the distal or post-arterial branches become the ileocolic and right colic arteries and the distal part of the mid-gut becomes the proximal colon. The importance of this disposition lies in the fact that a voluminous gut with its mesentery is attached by a very narrow pedicle upon which it may swing and rotate with ease.

At the fourth week of intra uterine life the greater part of the mid gut is extruded from the abdominal cavity by the increase in size of the liver and other organs, and the mid gut comes to lie within

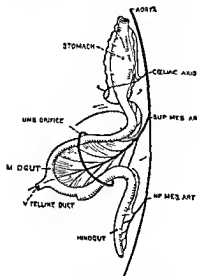


FIG 229 Intestinal rotation (1) Before the first stage (After N M Dott)

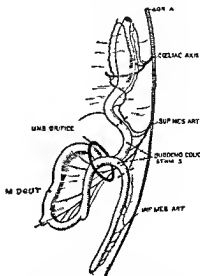


FIG 230 Intestinal rotation (2) Completion of first stage (lateral view) (After N M Dott)

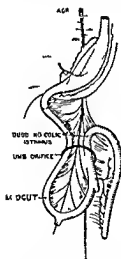


FIG 231 Intestinal rotation (3) Completion of first stage (anterior view) (After N M Dott)

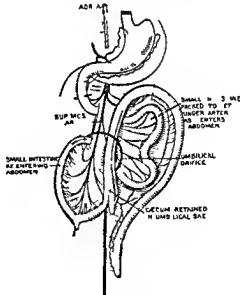


FIG 232 Intestinal rotation (4) Second stage in progress (After N M Dott)

the umbilical cord—a "physiological hernia". Rarely such a hernia persists (exomphalos). The principal stage of the normal process of rotation occurs when this hernia is reduced for the re-entering intestines become subject to various mechanical factors inside the abdomen.

The first stage is a simple one, and consists in anti clockwise rotation of the whole mid gut loop through 90 degrees. The growing

stomach projects its pyloric end towards the right side of the mid line, and thus carries the proximal end of the mid-gut to the right. The base of the mid-gut loop now lies transversely with the duodenal papilla and the left colic flexure at almost the same level, and the small intestine lies to the right of the mid line, the proximal colon to the left (*see Fig. 230*).

*The second stage* includes the crucial phase of the process of rotation. It takes place at the beginning of the tenth week, when the mid-gut returns from the umbilical cord into the general body cavity, and its normal progress depends upon various mechanical influences to which the gut then becomes subjected. Its effect is to rotate the mid-gut loop through a further 180 degrees in the anti-clockwise direction.

The first part of the mid-gut to return to the abdomen is the proximal end, the duodenum and jejunum, which returns in the line of its long axis. The cæcum, owing to its bulk, is the last portion to be reduced, and while it lies in the umbilical cord it exerts an important influence upon the rotation process, for it holds the superior mesenteric artery tautly forwards and thus provides an axis around which the small intestine may rotate.

When the re-entering coils of duodenum and jejunum (at present lying to right of the mid line) reach the abdomen, they meet the resistance of the liver and they are deflected downwards on the right side. With further deflection in the same (anti-clockwise) direction they become propelled behind the taut axis of the superior mesenteric artery and thus the uppermost coil, the terminal duodenum, comes to lie transversely below and behind this vessel. The jejunum and ileum follow the same course, and when eventually the cæcum returns to the abdomen the whole small intestine lies on the left side, and the proximal colon is displaced to the right (*see Figs. 232 and 233*).

*The third stage* which is a less complicated one, concerns the descent of the cæcum and proximal colon to their adult position, and the subsequent fixation of the intestinal mass.

At the conclusion of the second stage the cæcum, now returned to the abdominal cavity, lies immediately deep to the umbilicus. By various mechanical influences the cæcum is propelled upwards and to the right to reach the subhepatic region, whence it migrates to reach its adult position in the right iliac fossa.

Up to this point the whole mid-gut remains suspended in its fan-shaped mesentery from the duodeno-colic isthmus, but now certain parts of it become fixed to the dorsal abdominal wall. That part of the mesentery which encloses the superior mesenteric artery becomes adherent to the dorsal wall along an oblique line extending towards the right iliac fossa, and this line subsequently is known as the *root of the mesentery*. In this process the duodenum becomes fixed where it passes beneath the artery, and it thus acquires its retroperitoneal position. Lastly the post-arterial mesentery, containing the right colic and ileo-colic vessels, fuses with the posterior parietes, and the proximal colon thus becomes fixed.

**Derangements of Rotation.** Derangements of the first stage are very rare, while those of the third stage are so frequent as to be common place. The most interesting though rare anomalies are those of the

second stage. These have been classified by Dott in three principal groups as follows :—

(1) *Non-rotation*. Here the gut as it enters the abdomen fails to rotate, and the small intestine remains on the right, the proximal colon on the left. The duodenum does not pass horizontally across the abdomen, but passes directly downwards, and the coils of jejunum lie close below the liver. The lower part of the ileum crosses the midline and enters the right side of the cæcum. The ascending colon lies to the left of the midline, and the transverse colon, which is short, is related to the left part of the greater curvature of the stomach.

The anomaly of non-rotation is of great practical importance, for

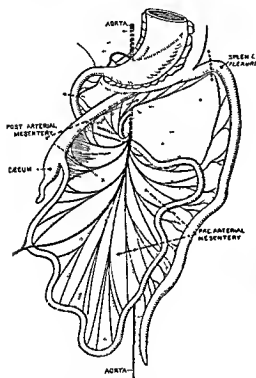


FIG 233. Intestinal rotation. (5) Second stage completed (After N. M. Dott)

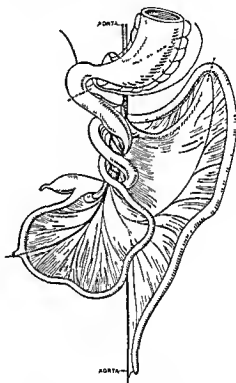


FIG 234. Anomaly of intestinal rotation. Volvulus neonatorum (After N. M. Dott)

as a result of it the cæcum and appendix are displaced and in diseases such as appendicitis the symptoms are left-sided. The anomaly is also important for its secondary effects, for the gut sometimes remains unfixed and unduly mobile. If the whole mid-gut remains free, suspended from its narrow duodeno-colic isthmus, it is very apt to undergo volvulus in the early days of life—*volvulus neonatorum* (see Fig. 234). This is a condition of great gravity. It differs from volvulus in adults in several particulars which may render its recognition, even at the time of operation, a matter of some difficulty. The whole mid-gut is affected, but since its lower end is less acutely twisted than its upper end, the gut remains collapsed, and the clinical features are those of duodenal obstruction, with little distension in the lower abdomen.

stomach projects its pyloric end towards the right side of the mid-line, and thus carries the proximal end of the mid-gut to the right. The base of the mid-gut loop now lies transversely with the duodenal papilla and the left colic flexure at almost the same level, and the small intestine lies to the right of the mid line the proximal colon to the left (see Fig. 230).

The second stage includes the crucial phase of the process of rotation. It takes place at the beginning of the tenth week, when the mid-gut returns from the umbilical cord into the general body cavity, and its normal progress depends upon various mechanical influences to which the gut then becomes subjected. Its effect is to rotate the mid-gut loop through a further 180 degrees in the anti-clockwise direction.

The first part of the mid-gut to return to the abdomen is the proximal end, the duodenum and jejunum, which returns in the line of its long axis. The cecum, owing to its bulk, is the last portion to be reduced, and while it lies in the umbilical cord it exerts an important influence upon the rotation process, for it holds the superior mesenteric artery tautly forwards and thus provides an axis around which the small intestine may rotate.

When the re-entering coils of duodenum and jejunum (at present lying to right of the mid line) reach the abdomen, they meet the resistance of the liver and they are deflected downwards on the right side. With further deflection in the same (anti-clockwise) direction they become propelled behind the taut axis of the superior mesenteric artery, and thus the uppermost coil, the terminal duodenum, comes to lie transversely below and behind this vessel. The jejunum and ileum follow the same course, and when eventually the cecum returns to the abdomen the whole small intestine lies on the left side, and the proximal colon is displaced to the right (see Figs. 232 and 233).

The third stage, which is a less complicated one, concerns the descent of the cecum and proximal colon to their adult position, and the subsequent fixation of the intestinal mass.

At the conclusion of the second stage the cecum, now returned to the abdominal cavity, lies immediately deep to the umbilicus. By various mechanical influences the cecum is propelled upwards and to the right to reach the subhepatic region whence it migrates to reach its adult position in the right iliac fossa.

Up to this point the whole mid-gut remains suspended in its fan-shaped mesentery from the duodeno-colic isthmus, but now certain parts of it become fixed to the dorsal abdominal wall. That part of the mesentery which encloses the superior mesenteric artery becomes adherent to the dorsal wall along an oblique line extending towards the right iliac fossa and this line subsequently is known as the root of the mesentery. In this process the duodenum becomes fixed where it passes beneath the artery, and it thus acquires its retroperitoneal position. Lastly the post arterial mesentery, containing the right colic and ileo-colic vessels fuses with the posterior parietes, and the proximal colon thus becomes fixed.

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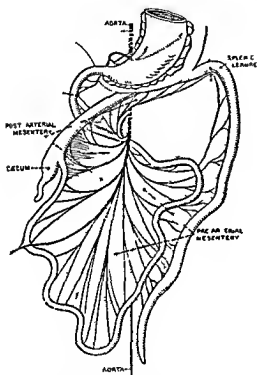


FIG 233 Intestinal rotation (5) Second stage completed (After N. M. Dott)

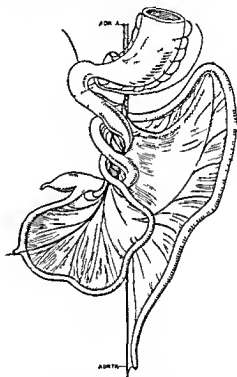


FIG 234 Anomaly of intestinal rotation Volvulus neonatorum (After N. M. Dott)

as a result of it the cæcum and appendix are displaced and in diseases such as appendicitis the symptoms are left sided The anomaly is also important for its secondary effects, for the gut sometimes remains unfixed and unduly mobile If the whole mid gut remains free, suspended from its narrow duodeno colic isthmus, it is very apt to undergo volvulus in the early days of life—*volvulus neonatorum* (see Fig 234) This is a condition of great gravity It differs from volvulus in adults in several particulars which may render its recognition, even at the time of operation, a matter of some difficulty The whole mid gut is affected, but since its lower end is less acutely twisted than its upper end, the gut remains collapsed, and the clinical features are those of duodenal obstruction, with little distension in the lower abdomen



Moreover since the blood supply is little affected the deep discoloration so characteristic of other forms of volvulus may be lacking. The condition should be suspected when a young infant, previously in good health, suddenly commences to vomit bile-stained material.

(2) *Reversed Rotation*. This is an interesting anomaly, which is believed to be due to the return of the proximal colon to the abdominal cavity *before* the jejunum. The proximal colon therefore is the first part to rotate, but in the reverse (clockwise) direction, and it comes to lie in the position normally occupied by the duodenum, often in a tunnel deep to the root of the mesentery of the small intestine. In spite of the altered rotation, however, the remainder of the gut eventually reaches the normal adult position. Clinically it is of importance, for the transverse colon may be constricted as it lies deep to the mesentery, and obstruction may result.

(3) *Malrotation*. This includes several irregular and less clearly understood defects of rotation, whereby part or the whole of the mid-gut may be displaced.

**Derangements of the Third Stage.** The commonest of these concern the descent of the cæcum and proximal colon, and their subsequent fixation. Failure of descent leads to fixation of the cæcum in the loin or close under the liver, and too prolonged descent, with lack of fixation, leads to all degrees of mobility of the cæcum and proximal colon. The appendix may remain high up in the loin in the retrocolic and retrocecal positions, and its tip may extend as far as the liver. When the proximal colon remains unfixed and floating it may undergo volvulus in adult life.

### ANOMALIES OF THE VITELLINE DUCT MECKEL'S DIVERTICULUM

The vitelline duct (or *volv stalk*) forms a communicating channel which in early life passes from the volv sac along the umbilical cord to the intestinal canal. In normal circumstances it is obliterated at about the sixth or seventh week of intra uterine life, but it may persist and cause trouble at a later date. The obliterative process begins at the umbilicus and extends to the intestine, and consequently the intestinal end of the duct persists most frequently. The common form is a small blind diverticulum projecting from the ileum a few feet above the ileocecal sphincter. The diverticulum may be finger like or rounded. It is usually two or three inches long and projects from the antimesenteric border of the gut, with its end free in the peritoneal cavity. Occasionally it arises on the mesenteric aspect and lies within the ileal mesentery. In its customary intraperitoneal situation it may terminate abruptly, with a rounded or conical end, or it may taper into a thin fibrous cord, attached by its other end to the mesentery. This cord represents the obliterated vitello-intestinal artery. To it the diverticulum owes much of its potential danger, for the cord may snare portions of intestine and so cause obstruction. Rarely a remnant of the vitelline vascular system may persist although the vitelline duct is completely obliterated. Thus a fibrous cord representing the vitelline

artery may pass from the umbilicus to the ileal mesentery, whilst the vitelline vein may be represented by a cord extending from the umbilicus towards the third part of the duodenum

The vitelline duct may remain patent through its whole length. Occasionally only the umbilical end remains, forming a small sinus, which discharges at the umbilicus, and it may prolapse on to the abdominal wall (the so-called enteroteratoma). An intermediate portion may persist and form a cystic swelling in the peritoneal cavity—entero cystoma. Rarely a portion abnormally placed in the mesentery may form an "enterogenous" type of mesenteric cyst (*see p 553*)

In some cases stenosis of the ileum may coexist, ranging from slight narrowing to complete obliteration. Sometimes there is a diaphragm of mucous membrane perforated by a mere slit. This may allow the passage of intestinal contents, but solid objects such as fruit stones are liable to become impacted.

**Complications** The complications of a persisting portion of the vitelline duct are legion, and there must be few surgeons who have had no experience of the remarkable intra abdominal entanglements to which it may give rise. For convenience they may be classified as (1) intrinsic primarily affecting the diverticulum itself, and (2) extrinsic, affecting other portions of the intestine.

(1) *Intrinsic Complications* Not uncommonly the communication between the diverticulum and the intestine is small and it may undergo progressive stenosis until completely occluded, so that the diverticulum dilates to form a cyst, which fills with mucoid material and may reach great size. Infection of the diverticulum may occur and simulate appendicitis. In exceptional cases an ulcer may form in the diverticulum and may give rise to hæmorrhage into the bowel or may perforate into the peritoneal cavity. The diverticular wall may contain traces of heterotopic gastric mucous membrane and the ulcer may thus be regarded as of peptic origin. Not infrequently simple tumours such as adenoma or myoma arise in the wall of a diverticulum.

(2) *Extrinsic Complications* These arise from the action of the whip-like fibrous cord attached to the apex of the diverticulum. The cord may be free at first but it is apt to contract adventitious adhesions and thus to provide a snare through which a hernia may occur. A diverticulum fixed to the umbilicus provides a fulcrum for volvulus of the intestine. Even if unfixed a dilated diverticulum may by its weight achieve the same result. Lastly, and very rarely a diverticulum may prolapse inside the ileum and lead to intussusception.

**Multiple Diverticula of the Small Intestine** Multiple diverticula occur, though rarely, in the jejunum or the ileum the latter situation being the more common. They may be present in large numbers affecting several feet of the gut. Unlike diverticula of the colon they project on the mesenteric aspect of the bowel, along the line of the blood vessels. They consist of mucous and submucous tissue alone protruding through gaps in the muscular tunic. It is generally assumed that they are developmental in origin though the suggestion has been made that they are pulsion diverticula arising from irregular peristaltic contractions and consequent increase in the pressure within the gut.

while the blood becomes increasingly concentrated and the total blood volume is much reduced.

Of the mineral elements, most attention has been paid to the chlorides, perhaps because they are so readily estimated. At an early stage chlorides disappear from the urine, while the blood chlorides are reduced from the normal of 500 mg % to as low as 350 mg. %

It is now recognized, however, that important as is the chloride deficit, the sodium loss is of greater significance, for whereas the chloride radicle is promptly replaced by bicarbonate there is no way of making good the loss of fixed base.

The loss of water and salts has profound effects, not only on the total body fluid, but also on the relative proportions in the blood stream, the tissue spaces and the fixed cells. These changes are described on p. 26. In addition the proteins are depleted, partly by loss in the vomit, partly by starvation. As a result of increased protein breakdown the non-protein nitrogen and urea content of the blood is raised, and in the later stages, this may be aggravated by impaired excretion due to renal damage.

**Effects of Distention of the Gut.** The distention of the bowel proximal to the obstruction is now recognized to play an important part in the constitutional upset which results.

The distention is at first mainly gaseous, due partly to swallowed air and partly to the products of fermentation. Whatever the primary character of the gas, it soon attains a fairly constant composition, containing about 70 to 80% of nitrogen, with the remainder made up principally of carbon dioxide and hydrogen sulphide. This is due to the fact that these gases are but little diffusible through the intestinal wall, whereas oxygen, which is highly diffusible, is quickly brought into equilibrium with the blood gases.

Distension of the bowel, however produced, may influence the general condition in three ways. Pressure upon the diaphragm if severe may affect the action of heart and lungs as is demonstrated readily by the prompt improvement which follows gastric lavage. Stimulation of afferent nerves in the wall or mesentery of the affected loop plays a part, not readily observed in ordinary forms of obstruction, but easily seen in an experimental closed loop, where distension with saline, or by means of a balloon gives rise immediately to pain, nausea, vomiting and collapse.

The most important influence of distension, however, is on the exchange of gases and fluids between the lumen and the blood. When a loop of intestine is distended the veins in its wall are compressed, particularly at the point where they enter the mesentery. The resulting venous stasis impedes the absorption of gas and fluid from the affected loop, and indeed may lead to exudation of fluid into the wall of the gut and the lumen. If a long segment is involved the resultant loss of fluid is considerable.

The part played by distension of the gut is of great importance in relation to treatment, and the value of deflation by gastric drainage or by a Miller-Abbott tube introduced into the small intestine is now well recognized. In the absence of strangulation, deflation combined

with fluid replacement will almost completely obviate the constitutional effects of obstruction, and indeed in experimental animals with high obstruction life can be prolonged by these methods for several weeks.

**Intestinal Toxins** Formerly a good deal of importance was attributed to the depressor effect of toxic substances elaborated either within the lumen or in the wall of the obstructed bowel, as a result either of bacterial proliferation or of breakdown of the protein content of the intestinal juices into toxic proteoses. The general opinion at the present time is that while undoubtedly such poisonous substances are formed in the stagnant contents of the distended gut, they can do little harm in view of the limited extent to which absorption can take place. They may possibly play some part, however, when the obstruction has been relieved and the contents are thus enabled to reach healthy intestine from which absorption readily occurs.

**Peritoneal Infection** A new factor comes into play when the bowel becomes devitalized, for then bacterial toxins from the stagnant intestinal contents escape into the peritoneal cavity and are readily absorbed into the blood stream. This development occurs at an early stage in strangulation, particularly if, as in an internal hernia, the whole strangulated loop lies within the peritoneal cavity. It may occur also though at a later stage, in simple obstruction where the combined effects of distension, venous stasis and bacterial proliferation have led to ulceration of the mucosa.

### Features of Special Types of Obstruction

**Simple Obstruction** It is now recognized that the effects of simple obstruction depend to a large extent upon the level of the blockage.

If the block is high that is to say, in the duodenum, below the bile papilla or in the upper reaches of the jejunum the effects are principally due to simple loss of water and electrolytes (and, to a smaller extent to the mechanical results of gastric distension). The beneficial effects of gastric drainage and fluid replacement give ample proof of this statement.

In simple obstruction at a low level, on the other hand, while loss of intestinal secretions remains important, there are in addition the factors which result from distension of extensive portions of the bowel and the consequent venous stasis within the bowel wall. These effects can only be countered (short of operation), by drainage through a Miller Abbott tube.

**Strangulation** Here to the effects of simple occlusion are added those of impaired blood supply. At first usually the venous drainage is alone involved. Consequently the affected loop becomes congested and heavy with blood and exudate, and if the strangulated loop is a large one a considerable depletion of the volume of blood in circulation results.

As the obstructing band tightens, consequent on swelling of the loop, the arterial supply also is cut off. At this stage necrosis of the bowel wall sets in rapidly and toxins will then leak into the peritoneal cavity, from which there is ready absorption into the blood stream.

As the necrosis proceeds bacteria also gain access and frank peritonitis results

The importance of these factors is well seen by comparing the progress of strangulation in an internal hernia with that of an external hernia. In an internal hernia the toxic changes appear early and assume grave proportions, for the toxins and the bacteria gain direct access to the general peritoneal cavity, on the other hand in external hernia, since there is little absorption from the inguinal or femoral sac, the toxæmia may be negligible even though the bowel is completely gangrenous. This must be borne in mind at operation on external hernia, when care must be taken to avoid contamination of the general peritoneal cavity by the highly toxic and infective content of the sac. Even more important, it must be remembered that even though the strangulated loop is not obviously non-viable its return to the peritoneal cavity may be fraught with grave risk.

**Closed-loop Obstruction** This type of obstruction is present in nearly all strangulations. In its pure form, that is without impairment of the blood supply, it is rarely seen under natural conditions.

Its effect is to aggravate the changes already described, particularly those changes due to tension within the affected loop.

**Paralytic (Adynamic) Ileus** This is a special type of obstruction in which there is no organic block, but a functional obstruction due to paralysis or disordered motility of the bowel. It occurs most often after abdominal operations and in relation to peritonitis.

The nature of paralytic ileus is best understood by considering the effect of abdominal operations on the intestinal movements. It is common knowledge that when the abdomen is opened under general anesthesia all movement ceases. After operation the paralysis persists for a period which depends upon the severity of the trauma that has been inflicted. Under spinal anesthesia, if high enough to implicate the splanchnic outflow, the intestinal movements during operation are on the other hand exaggerated, but transient paralysis occurs later when the anesthesia wears off.

Return to normal peristaltic activity does not occur normally throughout the intestines but segmentally, and the common "gas pains" of the post-operative period are due to irregular contractions with intervening segments of gas-filled bowel.

This physiological response to injury represents paralytic ileus in its simplest form. In more severe degree it may result from injuries causing retroperitoneal hemorrhage, from toxic states such as hepatic or renal failure or even from the application of a tight plaster jacket.

By far the most important cause of paralytic ileus however, is peritonitis, due for example to appendicitis or occurring as a complication of operation. The precise mechanism whereby peritonitis leads to paralysis of the bowel remains obscure, but it seems probable that the principal factor is direct damage to the nerve plexuses of Meissner and Auerbach and to the intestinal musculature by toxins diffusing from the peritoneum.

Since peritonitis generally affects the lower abdomen and pelvis the distal coils of ileum are most often involved, whereas the jejunum

escapes until a late stage. The secondary developments that take place are similar to those of a simple obstruction of the ileum to which must be added of course the toxic and infective complication of the peritoneal infection itself. If these effects can be combated by fluid replacement, intestinal drainage and chemotherapy, the paralysis will recover in due course and the intestinal motility be restored.

### INTUSSUSCEPTION

Intussusception is the invagination of one part of the intestine into the part immediately adjoining. It may occur at any age, but is commonest in healthy males during the first year of life. It is the most frequent cause of intestinal obstruction during early life. With few exceptions the invagination of the bowel is from above downwards and usually the terminal portion of the ileum is the part primarily affected.

**Ætiology.** In the majority of cases there is no obvious anatomical explanation and there is considerable evidence that the underlying cause is derangement of the normal peristaltic mechanism of the intestine, excited by errors in diet. Probably faulty diet is an exciting factor, for intussusception is especially prevalent in children of the poor, and has its greatest incidence between the fourth and seventh months of infancy when injudicious additions to the child's dietary are often made.

It has been suggested that in many cases there is an inherent defect in the neuromuscular coordination of the intestine, such as would allow a localized constriction, once formed to persist unduly, and favour invagination into a passive segment of bowel immediately beyond. In infancy the inhibitory nervous apparatus is developed latest, and it is apt to lag behind the motor, so that at an early age the inhibitory activities of the parasympathetic nerves are functionally weak and the tonicity of plain muscle outweighs for a time its capability of relaxation. Such inherent nervous disabilities in the gut may account for the frequency of intussusception in vigorous male babies with strong musculature as compared with puny children with atonic intestines, for its tendency to recur in some cases and for the rarity of the disease in adults. The neurogenic explanation is supported by the observation that intussusception may occur spontaneously in animals after paralysis of the intramural nerve plexus of the gut.

Structural peculiarities of the intestine also may favour the development of intussusception. Thus intussusceptions of the ileocaecal region are specially apt to develop if the ascending colon is unusually mobile owing to the abnormal presence of a mesocolon, and also lymphoid tissue is relatively excessive in that region and readily becomes swollen and congested.

In older children and in adults intussusception is generally initiated by some local lesion such as a polypus, a diverticulum, or an inflamed lymphoid patch. In adults it may begin at the site of a malignant growth, and is then probably brought on by the peristaltic effort of the intestine to pass the obstruction.

**Anatomy of an Intussusception.** As one part of the intestine

passes inside another the resulting intussusception is composed of three layers of intestine—entering returning and receiving, and on cross section these appear as three concentric tubes. The outer or receiving layer is known as the sheath or *intussuscipiens*, the entering and returning layers as the *intussusceptum*. The most advanced part of the intussusceptum where the entering and returning layers become continuous is known as the *apex*. The ring where the returning layer becomes continuous with the sheath is known as the *neck*. The entering and returning layers have their serous surfaces opposed but usually they are partly separated by that portion of the mesentery which is drawn in as the intussusception proceeds.

#### Method of Progression

The apex of an intussusceptum is formed of the same segment of intestine from first to last. That segment is the starting point it speedily becomes congested and swollen and constitutes a partial obstruction. The peristalsis behind it striving to overcome the obstruction drives it onwards as though it were a foreign body into the part of the intestine beyond invaginating that part. The congestion and œdema make this apical segment so stiff that the inner tube cannot roll round and become part of the middle or returning layer and therefore as the invagination proceeds the middle layer is increased wholly at the expense of the outer layer or sheath. The process of indrawing of the sheath and consequent elongation of the returning layer is unretarded until tension is put upon the mesentery, and after that onward movement occurs by the stretching torsion or angulation of the mesentery at the neck of the intussusception. It is probable that the intermittent spasmodic pain characteristic of this disease is due to that traction. On account of the tension exerted through the mesentery the intussusception alters its position and becomes curved with its concavity towards the root of the mesentery. In

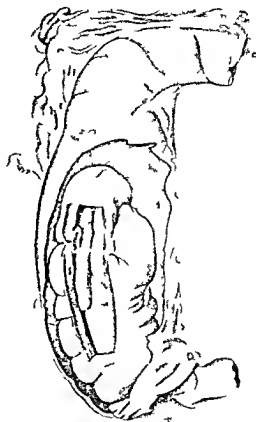


FIG. 93. Acute intussusception of ileocecal region.

(Department of Surgery, University of Edinburgh.)

cases where the invagination of the bowel is very great, as when an ileocecal intussusception reaches the rectum, the bowel frequently forms the arc of a circle, the centre of which is at the root of the mesentery and the increase in length of the intussusception is gained by the spiral torsion of the mesenteries.

On account of the dragging effect of the mesentery, the apex of an intussusception may become tilted and its orifice oblique or eccentric, and the free antimesenteric border of the returning part may then slip down for an inch or two beyond the true apex. This phenomenon is most often observed in intussusception of the ileocecal region and in such cases, when reduction is brought about the colic valve will appear before the cæcum, which is found to be "dumpled" on its serous aspect from being dragged down in advance of the apex.

**Pathological Effects of Intussusception.** The most important pathological effects of intussusception are due to occlusion of the blood vessels in the mesentery of the affected part of the intestine, and intussusception is virtually intestinal obstruction with the risk of strangulation (q v).

The first effects are congestion and œdema from the impeded venous return—they are followed by the discharge of blood stained mucus into the bowel and long continued venous stagnation leads to thrombosis. The œdema is most marked at the apex and in the returning layer the apex becomes swollen and knob-shaped and may form an obstacle to reduction. Finally pressure is sufficient to occlude the arteries and then necrosis and gangrene of the invaginated bowel ensue. The vitality of the sheath is seldom imperilled. As a result of necrosis perforation of the bowel may occur. In rare cases after gangrene has set in the necrosed intussusceptum may be extruded from the bowel as a slough, resulting in spontaneous cure.

The rapidity of these changes varies and, therefore, acute, subacute, and chronic types of intussusception are recognized.

### Special Types of Intussusception

(a) Ileocolic is the commonest variety of intussusception especially in infants. The invagination usually begins in the last few inches of the ileum and the apex passes through the ileocecal orifice. As the intussusception increases at the expense of the colon the ileocecal valve and the appendix become invaginated—ileo-ileocolic type.

(b) Enteric intussusceptions, originating in the small intestine, are rare in infants but may occur in adults as a result of the presence of a tumour.

(c) Double intussusceptions are those in which the sheath has become folded upon itself. They are almost invariably found in intussusceptions beginning at the lower end of the ileum or at the ileocecal valve. Triple intussusception also may occur.

(d) Retrograde intussusceptions are those in which the lower part of the bowel is invaginated into the part above. They have been most often found in the jejunum and in the transverse and descending colon. Sometimes they have been observed at post mortem following a blow on the abdomen. The intussusception may be multiple. Several cases



of retrograde intussusception of the jejunum into the stomach through the orifice of a gastro jejunostomy have been reported (*see* p 472)

(e) Chronic intussusception may occur as a primary condition in infants and in adults. It is usually of an ileocolic type. The intussusception may persist for months or even years. Adhesions may form between the invaginated coils of intestine and render it irreducible, but often there are no adhesions. Ulceration of the implicated coils of intestine is common and the sheath may become perforated at several points. Chronic intussusception gives rise to paroxysms of intestinal colic attended by tenesmus and mucoid discharge from the colon. It may culminate in acute obstruction.

(f) Intussusception of the appendix is very rare. The invagination may begin at any point in the appendix, or partial or complete inversion of the appendix into the cæcum may occur followed sometimes by colonic intussusception. In some of the reported cases, pathological conditions of the appendix, such as new growths, mucocoele and concretions, have been responsible.

## TUBERCULOSIS OF THE SMALL INTESTINE

Tuberculosis of the small intestine is not uncommon. It affects especially adolescents and young adults, and often it is accompanied by tuberculous lesions in the peritoneum and in the mesenteric lymph glands.

The disease is most common in the subjects of pulmonary tuberculosis, and is then attributable to infection by swallowed sputum. It is usually a grave complication. Sometimes there is no obvious affection of the lungs, and in such cases a milk borne infection may be responsible.

The distal part of the ileum is affected most often, for this is the most actively absorptive part of the gut and, in addition, is the part most richly supplied with lymphoid tissue. The disease arises first in the Peyer's patches and spreads thence to the neighbouring parts of the intestinal wall, forming ulcers of typical tuberculous characters, with pale granulating bases and undermined edges. The ulcers extend in the direction of the lymph drainage and consequently they become elongated and lie at right angles to the long axis of the gut. Sloughing is much less in evidence than in typhoid ulcers.

Tuberculous ulcers of the intestine rarely perforate, and their chief surgical importance lies in the fact that in healing by fibrosis they tend to constrict the lumen of the gut and to give rise to strictures. Such strictures may be single, but often are multiple. Since the intestinal content is fluid they give rise to no symptoms during a long period, but eventually they tend to cause chronic and finally acute obstruction. Obstruction may be precipitated by the impaction of a foreign body such as a fruit stone, a gall stone, or inspissated fæces.

Not infrequently in its acute phases a tuberculous ulcer of the intestine may lead to infection of the peritoneum and to the formation of peritoneal adhesions, and these subsequently may give rise to symptoms by exerting traction upon the intestine or by causing obstruction. All these manifestations are now rare.

## ULCERS OF THE SMALL INTESTINE

Apart from peptic ulcers of the duodenum and tuberculous ulcers of the ileum, ulceration of the small intestine is somewhat uncommon. In the majority of cases it is attributable to some definite predisposing condition, and in this category come jejunal ulcers after gastro-jejunostomy, dysenteric and typhoid ulcers, malignant ulcers, and, rarely, stercoral ulcers in the intestine proximal to an obstruction.

There remains a rare but interesting type of ulcer, the so called *simple ulcer of the small intestine*. This is a shallow erosion, which affects especially the ileum and generally appears to arise in one of the Peyer's patches. It appears to have an especial tendency to perforate acutely, when it gives rise to fulminating and often fatal peritonitis. The cause of such ulcers is not known. In some cases microscopic examination gives evidence of heterotopic gastric mucous membrane in the small intestine and it is possible that the ulcers may be due to such an anomaly and be thus comparable to peptic ulcers of the stomach or the duodenum. In other cases the ileum contains faecal masses that have regurgitated through an incompetent ileocaecal sphincter, and the ulcer may be attributable to the abrasion and infection thus induced. In others again the ulcer may result from regional ileitis (*see below*).

## REGIONAL ILEITIS

This is a non-specific inflammatory process involving a limited segment—from a few inches to a few feet in length—of the intestinal tract. It would appear that the disease has become commoner during the last decade. In the majority of cases it affects the terminal part of the ileum, sometimes encroaching upon the ileocaecal valve and caecum. Less often it affects a segment higher in the small intestine or in the colon.

At first there is a subacute inflammatory reaction in the wall of the affected part, which becomes swollen with oedema and very congested. The inflammation progresses to ulceration of the mucosa and subsequently to fibrosis with formation of multiple strictures. In severe cases the ulcers penetrate deeply into the intestinal wall, and they may perforate giving rise to a fulminating form of diffuse peritonitis. More often the inflamed part is walled in by adhesions of omentum and adjacent intestinal coils, so that when the ulcer perforates a localized abscess results. Such an abscess is very apt to spread to the surface and burst, giving rise to a faecal fistula—a complication which is especially apt to occur after an exploratory operation.

The naked eye appearance is characteristic. In the florid, active stage the affected loop of intestine is swollen, soft and spongy with oedema, and is greatly congested. The adjacent mesentery also is oedematous, and contains numerous enlarged glands of soft fleshy consistency. When the intestine is opened, its mucous membrane is seen to be swollen and inflamed, its villi and folds submerged in the general oedema. Multiple irregular ulcers are generally present, and the intervening mucous membrane may present swollen tags like inflamed polyp

In the later stages the congestion and œdema are less marked and the segment becomes tough and fibrous with multiple strictures. At this stage it closely resembles the hyperplastic form of ileocaecal tuberculosis.

Microscopic examination reveals various degrees of acute and sub acute chronic inflammatory change, non specific in character. There is an infiltration of inflammatory cells and according to the stage of the process polymorph leucocytes, lymphocytes or plasma cells may predominate. In the chronic phase foreign body giant cells may occur. They are liable to be mistaken for tubercle giant cells.

The cause of regional ileitis is not fully understood. It has been attributed variously to streptococci, coliform and dysenteric organisms, and more recently to sarcoidosis. At present proof of a specific infecting agent is lacking.

## TUMOURS OF THE SMALL INTESTINE

The small intestine is an uncommon site for tumours. Simple papillary adenoma, either single or multiple may grow from the mucous membrane and form polypoidal lobulated growths. Leiomyomata occur, and are often multiple. They form rounded, pedunculated tumours which project into the lumen of the gut. They may undergo malignant change and give rise to leiomyosarcoma. Fibroma, lipoma and lymphoma and argentophil tumours may occur. The special importance of simple tumours of the small intestine is that they frequently give rise to intussusception. Indeed, the vast majority of intussusceptions occurring after infancy are due to this cause. Of malignant tumours an adenocarcinoma is the most common. It occurs in the ileum more frequently than in the jejunum and forms a small white scirrhous growth which tends to encircle the gut, and may form a complete ring stricture. Since the intestinal content is fluid symptoms of obstruction develop only at a late stage. Sarcoma also may occur in the small intestine either as a primary growth generally a lympho sarcoma, or as a myosarcoma developing in a simple muscle tumour. Sarcoma tends to form a more massive growth,



FIG. 236. Carcinoma of the jejunum.

The tumour is of scirrhous nature and forms a small pale hard mass which has encircled the gut and has given rise to a very narrow stricture.

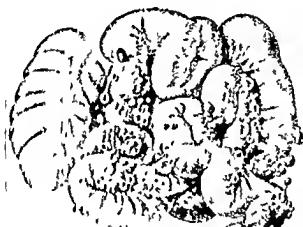
(Department of Surgery, University of Edinburgh.)

and as ~~not~~ it does not contract the bowel it is less likely to give rise to obstruction.

**Argemastine Tumours of the Small Intestine.** This type of tumour resembles the carcinoma of the appendix and is most common in the terminal portion of the ileum where it is often responsible for obstruction. It has occurred in a diverticulum. An argemastine tumour resembles a carcinoma in that it invades the tissues locally and may extend into the regional lymph glands. The tumour is yellow in colour and of firm consistency without any tendency to necrosis. Experience has proved that removal of the tumour and of invaded lymph glands gives permanent immunity to recurrence, unless, as rarely, the liver is involved.

### ENTERIC PNEUMATOSIS (Gas Cysts of the Intestine)

This rare condition is characterized by the development of multiple gas containing cysts in the subserous coats of the intestine. The cysts lie principally in relation to the ileum, but not uncommonly they extend over the whole length of the small intestine or even over the cæcum and



Gas cysts are rare in man, and are usually found by chance on exploration of the abdomen for gastric or duodenal ulcer or, less often, other diseases. Occasionally cysts of similar nature occur in the vaginal wall in pregnancy.

Enteric pneumatosis gives rise to no symptoms, and is of no clinical importance, but its puzzling aetiology has attracted much speculation, and several ingenious theories have been advanced. It has been suggested that the gas is a product of aerogenic organisms, but this is not supported by bacteriological evidence. Many authors have suggested that the origin of the cysts is mechanical, and that gas of intestinal origin is forced through minute fissures in the mucous membrane as a result of vomiting, or irregular peristaltic action, but against this view is the absence of intestinal flora within the cysts.

Masson in a valuable paper has supported the view of a chemical origin. He affirms that the cysts are dilated lymph or chyliferous channels, and that the gas is derived from chyle by chemical interaction with acid products of intestinal fermentation. In support of this view he points out, firstly, that chyle contains large quantities of carbon dioxide in the form of alkaline carbonates, and, secondly, that gas cysts occur most often in conditions associated with increased intestinal acidity. Presumably a carbon dioxide set free in this manner is subsequently replaced by nitrogen diffused from the blood, just as oxygen introduced into the pleural cavity may be replaced.

It is interesting to observe that enteric pneumatosis is common in swine fed on dairy refuse, and it is thought that the large quantities of lactic acid consumed provide the basis for the gas production.

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## CHAPTER XXV

### DISEASES OF THE COLON

#### CONGENITAL ABNORMALITIES OF THE COLON

##### Congenital Microcolon

IN this rare condition the entire colon with the exception of the rectum is extremely small, and its lumen may scarcely admit a quill. Though reduced in calibre its anatomical structure is perfect, it is a colon in miniature. The ileocaecal valve is normal but the small intestine is hypertrophied and contains putty like masses of meconium. Other congenital abnormalities such as atresia or absence of a segment of intestine may coexist.

Although many theories have been advanced, the origin of congenital microcolon, like that of other developmental errors of the intestines, is not understood. The condition results in acute obstruction soon after birth. Ileostomy offers the only means of relief, but in the early days of life leads to progressive dehydration which is not survived.

##### Congenital Megacolon (Hirschsprung's Disease)

The outstanding feature of this disease is that the colon, which is dilated and hypertrophied, is from birth or soon afterwards unable to evacuate its contents in a normal fashion, although there is no organic obstruction of its lumen. Male children are affected more often than females in the proportion of five to one.

**Morbid Anatomy** The dilatation of the colon is usually most extreme in the sigmoid portion and in about 37% of cases is confined to that part. In 34% of cases the upper part or the entire rectum<sup>1</sup> is also affected. In others the dilatation may extend to the descending or transverse part of the colon, and in about 25% it reaches the ileocaecal valve. The small intestine, however, is never affected. Cases have been observed in which only the proximal parts of the colon (ascending and transverse colon) have been affected. In many cases, at least 10%, there is an associated dilatation of the bladder. In exaggerated cases the dilated colon may have a diameter of 15 centimetres or more. In addition to dilatation, the affected part of the colon shows great hypertrophy of its walls, chiefly of the circular muscle, the teniae are less evident than normally. The serous coat also is

<sup>1</sup> Hurst believed that in nearly all cases the obstruction (due to achalasia) is situated at the sphincter ani and that the thick walls of the fixed rectum yield less readily than the relatively thin coats of the freely movable pelvic colon so that the rectum especially its lower half does not show the same degree of dilatation. His claims are supported by the finding of muscular hypertrophy of the rectum in a large proportion of the cases which have been examined post mortem.

thickened, and the mesentery of the colon is elongated to a considerable extent, and its vessels and nerves are hypertrophied.

The colon is greatly distended, aggravated by the accumulation of gas. It usually contains a large quantity of pultaceous, scybulous or offensive feces. The mucous membrane is cedematous and in a state of chronic catarrhal inflammation, and is often ulcerated.

Microscopic examination of the wall of the colon shows enormous hypertrophy of the circular muscle, and a variable degree of chronic interstitial colitis, evidenced by fibrous tissue hyperplasia and round-cell infiltration. Degenerative changes in the intramural nerve plexus (Auerbach) have been frequently observed, but whether primary or secondary is still debated.

Whether the distal limit of the dilatation is at the pelvic rectal junction or the internal sphincter of the anus there is no muscular hypertrophy at these points, nor is there any evidence of mechanical or spasmodic constriction. This is indicated by the observation that a finger or an instrument may be inserted beyond them without encountering resistance.

**Pathological Effects.** Obstinate constipation is the most obvious effect of congenital megacolon. Many days or even weeks may elapse without an evacuation of any kind being secured, and relief is usually obtained only by extraneous help. In some cases a certain amount of loose offensive fecal matter is passed each day, but constipation still persists and the bulk of the intestinal contents is often retained, likewise fluid introduced into the colon by a rectal tube is retained.

Megacolon varies in degree and in the age at which it becomes evident. In many, gross distension of the abdomen and visible peristaltic waves are present in the first few weeks of life. In others, progressive tumidity and obstinate constipation persist during months or years. In less severe cases, the only signs of the affection may be a slight, persistent abdominal distension and chronic constipation, which may persist into adult life.

As the disease progresses, distension may assume immense proportions and the abdominal muscles become thin from stretching, the diaphragm (especially on the left side) greatly elevated, and the costal angle widened and its margins everted. The general nutrition suffers, and emaciation, anemia, and debility ensue. If untreated a fatal issue frequently results in childhood from toxemia and anemia. Sometimes complications such as perforation of the colon, intestinal obstruction from strangulation, and intussusception develop, and usually prove fatal.

**Ætiology.** It is now generally agreed that the dilatation and hypertrophy in megacolon are not due to mechanical obstruction as by valves or by kinking of the colon. It is true that the pelvic rectal junction may become kinked, but this is believed to be caused by sagging of the elongated colon and is a result, not a cause of the obstruction.

The explanation most compatible with the pathological and clinical features is one which relates the disease to neuro-muscular incoordination resulting from a relative sympathetic overaction. The distal



part of the colon, like the rest of the alimentary canal, is controlled by the autonomic nervous system, from which it receives both para sympathetic and sympathetic fibres. Its parasympathetic supply, which is propulsive in action, is derived from the pelvic visceral nerves which emerge from the sacral nerve roots; its sympathetic supply, which maintains the normal tone of its sphincters, is derived mainly from the lumbar splanchnic nerves of each side, and is distributed along the inferior mesenteric artery and *via* the hypogastric plexus. In congenital megacolon it would appear that the normal coordination between the two systems—emptying and filling—is disturbed, and that there is a relative overaction of the sympathetic which exaggerates the normal tone of the sphincters which remain closed, not from spasm, but from inability to relax. Recent clinical and experimental observations have substantiated the validity of this hypothesis. In megacolon, elimination of the sympathetic nerve fibres of the distal colon is generally followed by relief of the obstruction, but the long established distensibility of the colon persists.

### ILEOCÆCAL TUBERCULOSIS

Compared with the small intestine the colon is rarely the site of tuberculosis, and when infection occurs it is almost always of the ileo cæcal region. The resulting lesion mimics cancer very closely, but its pathological features are very characteristic. It assumes a chronic and hyperplastic form, and occurs in adults between the ages of twenty and forty years. It is rare under ten years, and still more so after the age of sixty. For a reason that is not obvious females are more frequently the subjects of this form of tuberculosis than males. Often there is a familial history of tuberculosis.

**Ætiology.** It is generally conceded that this variety of intestinal tuberculosis constitutes a primary lesion, in that there is rarely any evidence of active tuberculosis elsewhere. Whereas tuberculosis of the ulcerative type in the small intestine is of quite usual occurrence in patients with pulmonary tuberculosis, ileo cæcal tuberculosis is very rare.

It is suggested that ingestion of tubercle bacilli is the common mode of infection. The occasional presence of ulcers in the colon, infection of the mesenteric lymph glands, and coincident strictures in the small intestine lend mild support to this mode of origin. The bovine type of tubercle bacillus is held to be responsible.

**Morbid Anatomy.** The process begins in the submucous or subserous coat of the colon, where follicles develop amidst an area of round cell infiltration. Tubercle bacilli cannot be demonstrated, and it is for that reason that some observers have doubted the specific nature of the disease and ascribe many examples to chronic regional enteritis, which it certainly resembles in many respects. Tissue reaction causes abundant proliferation of fibrous tissue, especially in the submucous layer, but often pervading all the coats. Fibrosis is the outstanding pathological feature of the affection, though excision may occur, but is very rare. The disease generally starts in the cæcum and it may extend towards the hepatic flexure. The ileum is sometimes involved, and the

appendix, which is often retracted towards the cæcum so that it is scarcely recognizable, seldom entirely escapes.

The diseased portion of the colon shows general thickening and coarseness of all its coats, which with much deposition of fat and infiltration

of the mesocolon may give rise to an obvious tumour. Contracture of the mesentery causes puckering of the bowel, which becomes fixed and rigid, and the colon becomes shortened and drawn towards the liver, and, as a result, the ileo-cæcal angle becomes obtuse. The adjacent lymph glands are usually enlarged and may be caseous or calcified.

From contraction of the fibrous tissue the lumen of the colon is reduced to a narrow channel, sometimes at a localized area, but more often over a considerable length. The colic valve is shrivelled and rigid, and may be difficult to identify. The small intestine often is affected by multiple strictures.

The mucous membrane of the colon is thick and oedematous and commonly is thrown into polypoidal folds. Sometimes there are large superficial ulcers with rather raised edges, situated either in the affected part of the bowel or somewhat distal to it; cicatrization of these ulcers may produce strictures of the lumen.

A combination of tuberculosis and carcinoma has been observed in a number of instances, and generally it would seem that a tuberculous infection had been the primary lesion and the cancer of later development.

The effect of ileocaecal tuberculosis is usually to cause obstruction but acute symptoms may be long

deferred. In some acute obstruction has followed impaction of foreign bodies such as a gall-stone or fruit stone. Perforation of a tuberculous cæcum is rare. Diagnosis of ileocaecal tuberculosis may be difficult on account of its close resemblance to cancer. Diarrhoea and melæna are seldom present. Formation of a cold abscess or of a fecal fistula several months after removal of the appendix is not an uncommon way in which the underlying disease may be revealed.



FIG 235. Ileocaecal tuberculosis. The wall of the cæcum and of the distal part of the ileum is greatly thickened as a result of fibrous and fatty infiltration. The ileum enters the cæcum at a very obtuse angle. Acute obstruction followed impaction of a plum stone at the stricture.

Chronicity of the symptoms, often with long periods of intermission, may help to suggest the diagnosis. A barium enema may prove helpful by indicating stenosis of the colon over an unusually wide area and the approximation of the ileocaecal region towards the costal margin.

At operation recognition of the tuberculous nature of the lesion may be impossible, unless some additional feature such as caseous glands or stricture of the ileum is present to lend confirmation.

As the effects of this type of lesion are mechanical, extirpation of the diseased segment of intestine is the method of choice, and, as the lesion is generally an isolated one, surgical treatment has no contra-indication.

**Tuberculous Colitis.** In rare instances the mucous membrane of the colon becomes the seat of widespread tuberculous ulceration. It affects the distal colon and the rectum, which become greatly thickened and oedematous. Though resolution may occur, the disease tends to pursue a very chronic course and often leads to widespread stenosis of the bowel. Cold abscesses and fistulae complicate the disease in many instances.

## DIVERTICULA OF THE COLON

Diverticula of the colon are present in at least 5% of patients over forty years, though they may produce no symptoms and are often discovered accidentally.

Diverticula occur in adults, and males are affected more often than females in the proportion of 2 : 1. The pelvic colon is the commonest site and may be the only part affected, but quite frequently the transverse and the descending colon are involved. The caecum and ascending colon are seldom the site of diverticula.

The early features of the disease shown by repeated radiographic examinations, suggest that there are three stages in the development and progress of the disease: (1) a pre-diverticular stage, (2) a stage of formed diverticula—diverticulosis, and (3) a stage when inflammatory changes have occurred—diverticulitis. The early stage may be noted to pass gradually to a more advanced one, or all stages may be present in different parts of the bowel or in a segment of it.

**Ætiology.** The common occurrence of diverticula at potentially weak points in its wall, such as the point of entry of blood or lymph vessels, supports the belief that they are of the nature of pulsion diverticula, formed as a result of abnormal pressure within the bowel, augmented, maybe, by bacterial infection of the walls and spasm of its circular muscle fibres.

Constipation has been blamed as an important factor in the production of diverticula, on account of the increased tension it imposes on the wall of the colon, but it is present in only half the cases. Spriggs believes that irritation caused by injudicious purgation with resulting stagnation of liquid feces in the sigmoid is a more likely cause.

The frequency of diverticula in stout subjects suggests that

infiltration of the muscular coat of the colon with fat leads to localized weakness which favours pouch formation

Irregular sustained contraction of the colon precedes the formation of diverticula as evidenced by the radiographic appearances of early cases. Probably in many subjects an inherent weakness of the walls of the colon predisposes to the occurrence of diverticula.



FIG. 230. Diverticulitis. The colon is segmented in a ladder-like fashion and all the coats are the seat of fibrous tissue proliferation.

(By courtesy of Mr J W S. R. H. H. S.)

**Pathological Features.** Early stages of the formation of diverticula are best demonstrated in radiograms after a barium enema. One of the first changes is that the affected part loses its normal segmentation and presents a more rigid and spastic outline. Small bead-like projections of recently formed pouches may be detected at several points and after a variable period diverticula may appear in parts of the colon which previously showed only spasticity. In the early stages the pouches are globular in outline and their necks relatively wide which allows faecal matter to enter and leave them freely. Later the pouches are flask-shaped and their necks are comparatively narrow.

In the early stages the only evidence of diverticulum formation is a slight superficial corrugation of the serous surface of the bowel. In typical cases at a later stage, the colon is studded with pea-like projections often coated with fat. Only the larger pouches are detectable on the exterior. Any part of the circumference of the bowel may be affected but points of entry of blood vessels and the appendices epiploicae are favourite sites and the transverse colon is rarely affected. Each diverticulum consists of a protrusion of mucous membrane into or through the muscular coat, and in all but the smaller pouches muscle fibres are present only at the neck. Pellets of inspissated faeces sometimes form in the interior of diverticula (stercoliths) and may cast a shadow visible on radiography. Seen from the interior the mouths of the diverticula may be circular or slit-like but more often on account of inflammatory oedema of the mucous membrane they can be detected only when the bowel is stretched or when faecal matter is expressed from them. Localized thinning of the colon is noted at the neighbourhood of the most recently formed diverticula.

Secondary inflammatory changes in the walls of the diverticula (diverticulitis) and in the adjacent colon (peridiverticulitis) are common and it is from these changes that symptoms commonly arise. The inflammatory changes are often slight and are associated with a round cell infiltration and fibrous tissue proliferation, and what is

very characteristic, the accumulation of quantities of fibro fatty tissue. The overgrowth of fibrous tissue and fat is most evident in the appendices epiploicæ, in the mesenteries, and in the subserous or the submucous coats of the bowel and is often so great as to conceal the diverticula completely. Contraction of the newly formed fibrous tissue may lead to stenosis of a segment of the colon, or may involve a considerable portion, giving it a rope like and rigid appearance. When stenosis becomes extreme, acute or chronic intestinal obstruction may result. Similar changes cause shortening of the meso colon and lead to abnormal fixation or to angulation of the colon, and increase the difficulties of operation. Contraction of fibrous tissue around the neck of the diverticula leads to retention of faecal matter and favours the occurrence of inflammation. Ulceration of a diverticulum by infection may terminate in perforation and lead to general peritonitis, or more commonly a localized abscess. The abscess usually points in the left iliac fossa, but it may perforate the bladder and form a colovesical fistula. In rare instances extraperitoneal rupture of a diverticulum leads to emphysematous cellulitis, and the infection may follow fascial planes and reach the thigh.

Acute exacerbations are apt to occur in diverticulitis, and are often associated with a mild degree of local peritonitis with attacks of pain in the left side of the abdomen.

Subjects of diverticulitis commonly suffer from lumbago, from spondylitis, and from other chronic lesions of ligaments and joints.

Differentiation from malignant disease is difficult when diverticulitis gives rise to a palpable tumour. Cancer and diverticulitis have been coexistent occasionally, but the association is too infrequent to be of practical importance. In diverticulitis great help is obtained from radiographic examination after a barium enema. Barium may be retained in diverticula for many weeks.

The pathological changes in connexion with diverticulitis may be so widespread as to preclude resection, while the infection of the bowel wall renders it unsuitable for primary suture.

**Congenital Diverticulum of the Cæcum.** This type of diverticulum is rare. It is solitary and emerges from the colon on its medial aspect immediately above the ileocaecal valve. It is of developmental origin, usually small, and has a complete covering of muscles. The neck of the



FIG. 210. Portion of same specimen as depicted in Fig. 230, to show the orifices of the diverticula.

(By courtesy of Mr J. W. Struthers.)

diverticulum is narrow, a factor which predisposes it to inflammatory complications similar to those in appendicitis. In some instances the inflamed diverticulum becomes inseparably bound to the colon and a mass develops which may simulate carcinoma.

## SIMPLE TUMOURS OF THE COLON AND RECTUM

Simple connective-tissue tumours are rare in the large intestine. A submucous lipoma is commonest and generally occurs in the cæcum, where it may give rise to obstruction or simulate appendicitis.

Commoner and more important are the epithelial tumours, which take the form of papillomata. Dukes found that in 127 subjects post mortem they were present in 10%, the incidence increasing after the age of forty.

Papillomatous growths vary in appearance, and three types may be recognized: (1) a smooth pedunculated polypus; (2) a villous papilloma; and (3) diffuse polyposis.

A pedunculated polypus occurs frequently in the rectum of children. Arising as an adenoma of the mucous membrane it becomes pedunculated as a result of peristalsis and it may be protruded at the anus. Its surface is smooth or mulberry-like and its colour pink or red according to the degree of congestion. In children this tumour, which is adenomatous in structure, is simple; but in adults it shows a tendency to become malignant.

A villous papilloma may be flat or pedunculated. Its size varies from that of a pin's head to a large button; its surface may be smooth, shaggy, or mammillated. A papilloma is often solitary, or there may be several hundred scattered over a segment of the colon.

Microscopic examination shows epithelium composed of columnar



FIG. 241. Carcinoma of the pelvic colon. dual growths. Note the pedunculated papilloma above the distal tumour.

(Department of Surgery University of Edinburgh.)

cells supported by a core of connective tissue derived from the submucosa. The blood vessels are thin walled and often dilated.

**Diffuse Polyposis** When the colon is covered diffusely by papillomata the resulting disease is known as diffuse or multiple polyposis or colitis polyposa. The polypi are preceded by a generalised hypertrophy of the mucous membrane and submucosa, as though it were the seat of irritation. The descending and pelvic parts of the colon are the most often affected, but the cæcum and rectum may sometimes be involved.

Diffuse polyposis is a precancerous condition. It is common in childhood. Nothing definite is known of its aetiology, but it is well known that it is often hereditary, as also is the predisposition to cancer. The polyposis is accompanied by a variable degree of colitis, so that diarrhoea with blood in the stools is usual and may lead to great depletion.

**Relation to Cancer** Polypi and cancer in the colon frequently coexist. In specimens of cancer of the colon removed at operation Dukes found papillomata in 75%. They occurred generally adjacent to the tumour and were often numerous. Thus it appears that the association of benign papillomata and cancer in the colon is very important and more than accidental.

That a simple papilloma may occasionally become malignant is known, but more often the malignancy develops elsewhere in the bowel. The experiences of Lockhart Mummery afford evidence that an adenoma may herald the development of carcinoma. In a series of 50 cases, observed and treated for many years, carcinoma developed in no less than twelve.

## CANCER OF THE COLON

The colon is frequently affected by cancer. The disease arises in later life, and is usually of slow progress and metastasizes, if at all, at a late stage. Occasionally it affects younger persons and then progresses more rapidly and disseminates earlier.

In over 40% of cases the tumour affects the pelvic colon, less often it affects the ascending, the transverse and the descending colon (in that order of frequency). The cæcum proper (*i.e.*, the portion of the colon below the ileocaecal valve) and the splenic flexures are each affected in about 5% of cases. The hepatic flexure is a rare site. Occasionally there are two or even more tumours, apparently distinct, either a few centimetres apart or in different portions of the colon. Rarely the removal of one tumour is followed several months or even years later by the development of a second or even a third "primary" growth.

**Microscopic Structure** The carcinoma has the structure of columnar cell carcinoma, and the histological features vary somewhat according to the degree of differentiation of the cells and the amount of fibrous tissue stroma. Generally the columnar cells are arranged in irregular acini, but sometimes the acinar arrangement

is lacking and they lie in solid groups, interspersed with a scanty areolar stroma. Not infrequently the tumour undergoes mucoid (colloid) degeneration and this character is usually reproduced in metastases.

### Types of Cancer of the Colon

According to their naked-eye characters, two principal types of cancer of the colon are recognized, (1) the proliferative type, (2) the annular sclerosing type. The second is the commoner, although intermediate types are frequent.

(1) The proliferative type occurs usually in the cæcum or the ascending colon, less often in transverse and distal colon. It is a bulky

tumour, which projects into the lumen as an uneven, nodular mass. Its surface ulcerates, leading to hæmorrhage and infection. The tumour does not encircle the bowel, but obstructs rather in virtue of its bulk. Since the proximal part of the colon is capacious and its contents fluid, obstruction does not supervene until late, and in some the only effects during a long period are anæmia and cachexia aggravated by infection. The irritation from the tumour and the adjacent in-



FIG. 712. Adeno-carcinoma of the colon. The tumour is composed of columnar mucus-secreting cells disposed in irregular acini.

flamed mucous membrane may lead to diarrhoea with abundant mucus in the stool.

(2) The annular type occurs in its characteristic form in the distal part of the bowel especially in the pelvic colon but it may occur more proximally, for example, in the transverse colon or at the mid part of the ascending colon. It grows slowly, and forms a small tumour which does not project much into the lumen, but infiltrates the wall of the bowel, encircling it. On account of the slow infiltrating character and the accompanying fibrosis the tumour leads to a localized constriction of the colon, as by a cord (*ring stricture*). On the mucous surface the growth remains circumscribed, with little longitudinal extension and ulceration may be long delayed and never very extensive. The affected part is rendered stiff and its lumen may be reduced to a very fine channel.

On account of the absence of much ulceration this type for long



gives rise to little disturbance of health and generally the first effects are progressive and ultimately acute obstruction

### Pathological Effects

Mention has been made of several of the effects of colon tumours for example hæmorrhage and toxic absorption which are more pronounced in the proximal portion of the colon. Obstruction is most likely to occur in the annular type especially when it is situated in the distal part of the colon where the lumen is of small calibre and the faecal content solid. Generally, the obstruction arises insidiously and is evidenced by increasing constipation and progressive abdominal distension. Eventually obstruction may be complete, and frequently that seems to be the first evidence of the disease. Complete obstruction may be due to stenosis of the bowel but often it is precipitated by impaction of a faecal mass or foreign body in the narrowed part. On rare occasions obstruction results from intussusception of the affected segment into the bowel distally.

In progressive obstruction the gut proximal to the constriction is hypertrophied and later dilated. Dilatation affects especially the cæcum which is distended by fluid faecal matter and gas.

Putrefaction of retained faecal matter favours development of the stercoral ulcers which may give rise to localized peritonitis or may perforate causing fulminating diffuse peritonitis. Perforation of the cæcum is especially likely to occur when the abdomen is opened and the colon is deprived of the support of the abdominal walls. Longitudinal splits in the tænia coli occur frequently when there is great distension. Ulceration close to the site of cancer may cause infection of the retrocolic areolar tissues and may lead to an intraperitoneal or extraperitoneal abscess.

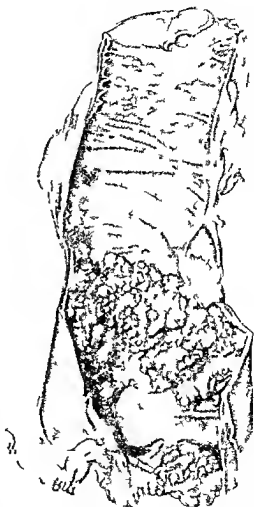


FIG 243 Papillomatous type of carcinoma of pelvic colon

### Avenues of Extension

Cancer of the colon generally grows slowly. It extends principally by direct infiltration of adjacent tissues and, later, by invasion of lymph vessels and glands. Metastasis to distant sites, such as the liver is a late feature.

*Direct Infiltration* At first the growth is limited to the mucous and submucous coats and in these layers it tends to spread mainly at right angles to the long axis of the gut. This is especially evident in the annular type of tumour. Later the growth penetrates the muscle coat and may erupt at the peritoneal surface or invade the retroperitoneal tissues and the muscles of the abdominal wall. In some cases a growth erupting at the peritoneal surface disseminates to many parts of the peritoneal cavity and gives rise to multiple metastases, especially in the omentum on the surface of the ovaries, or on the pelvic floor. In others as a result of superadded infection or direct infiltration, the affected portion of bowel becomes adherent to other viscera, particularly the small intestine or its mesentery, the bladder, or the uterus or its appendages so that at operation sacrifice of parts of these organs may be necessary.

*Lymph Spread* Tumours in the proximal and distal parts of the colon differ considerably in their paths of lymph vascular extension. The normal absorptive function of the proximal colon demands an abundant lymph drainage, and consequently there is a large number of glands in relation to this part. The distal colon, having no absorptive function possesses fewer glands.

For the colon the lymph vessels and glands are disposed along the main arteries. A few glands (epicolic) lie on the surface of the gut, but the more important ones lie within the mesenteries or in the retroperitoneal tissues. In the cæcum and the ascending colon the glands along the ileocolic vessels are involved, in the transverse colon the glands in the mesocolon and rarely, if the omentum is adherent, the gastro-epiploic glands, in the distal part of the colon the glands along the inferior mesenteric vessel and its branches are affected.

The differences in lymph drainage of the proximal and the distal colon are reflected in differences in the treatment and in the prognosis in the two situations. The numerous and relatively distant lymph glands in relation to the proximal colon necessitate a wider resection of the gut, and render subsequent recurrence more probable. The paucity of glands in relation to the distal colon justifies a local resection, and greater expectation of permanent freedom from disease.

*Blood Spread* Metastases by the blood stream seldom occur except in the advanced stages of the disease. Occasionally, however, they may do so earlier, and sometimes metastases develop in the liver, even before extension of the disease locally.

### STRICTURE OF THE RECTUM

Stricture of the rectum may result from traumatism or follow any type of ulcer, including malignant disease. Apart from these there is a type of rectal stricture which has long been recognised, though until

recently its aetiology was obscure. It nearly always occurs in women and originates as a hyperplastic fibrosis in and around the connective tissue of the rectum. In the course of years the scarring extends and leads to a long and eventually very tight stricture, situated usually 2 to 3 inches from the anus. The mucous membrane may remain free from ulceration until a late stage. Finally there may be fistule on the skin surface, and elephantiasis of the vulva may develop.

This type of stricture of the rectum was formerly ascribed to gonorrhoea or syphilis, but though it is possible that occasional cases have such an origin, recent observations prove that most are due to infection by the virus of lympho granuloma venereum. The infection, which is transmitted as a venereal disease, is seen most often in tropical or Mediterranean countries, but occasionally is brought to this country by persons returning from abroad. In man the rectal manifestation of the disease is rare and when it occurs a direct contagion may be assumed.

In diagnosis the Frei reaction (an allergic reaction induced by intradermal injection of extracts of fresh infective material) is almost specific.

## CARCINOMA OF THE RECTUM

Cancer of the rectum differs only slightly in its pathology from cancer in other parts of the colon, but on account of its position it is more convenient to consider it separately.

Carcinoma of the rectum is said to be four or five times as frequent as in the colon. It affects the two sexes with about equal frequency, and most often between forty and sixty years of age, although it is not very uncommon at an earlier age.

The growth begins generally at the pelvic rectal junction, where the tumour is just out of reach of an examining finger. It then grows

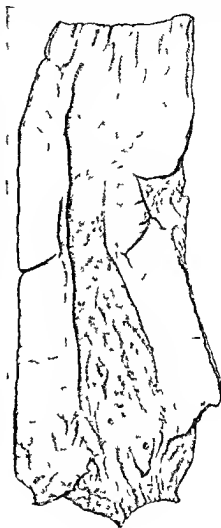


FIG 211 Stricture of the rectum. The lumen is narrowed by a stricture almost 3 inches in length. The mucous membrane is extensively ulcerated whilst the outer coats are infiltrated with a thick layer of dense fibrous tissue.

(By courtesy of Professor J. W. S. Blacklock.)

situated at, or just below, the peritoneal reflection. That relation is of importance because, when the growth abuts on the peritoneum, metastases may occasionally be diffused over a wide area by the subserous lymph vessels, or there may be a large plaque of disease in the peritoneum of the rectovesical pouch. Such highly placed growths are almost always of annular type, similar in character and in effects to those of the colon.

In the ampulla the cancer may be of a cauliflower type, or it may be sessile and extensively ulcerated. There are associated papillomata in about 30% of cases. Generally, tumours which grow towards the lumen of the bowel are less malignant than the flattened type which penetrates the rectal walls at an earlier stage. An exception to this general behaviour is the primary mucoid type of carcinoma, which is usually a bulky tumour of rapid growth, with marked invasive characters and a tendency to early metastasis in glands and by the blood stream.

Microscopically, the tumour is usually of columnar-cell type. There is considerable variation in different tumours, and in parts of the same tumour and examination of only part may lead to fallacious appendages. Within certain limits the histological appearances provide necessary reliable indication of its grade of malignancy. The common

*Lymph Spr.* one of ill formed acini or alveoli, composed of cells of colon differ considerably with many mitoses. More benign types may give the The normal appearance of simple adenoma. The mucoid type, which is the most abundant lymph composed of irregularly arranged cells distended with glands in relation totoplasm (signet ring pattern) it represents a malignant function, possesses of mucus forming cells, and is very malignant and

For the colon differentiated from the relatively benign types in which the main arteries. A differentiation is suggested by elaboration of mucus the more important acini of the tumour. peritoneal tissue. In many instances, carcinoma of the rectum is of relatively along the ileum and for long remains confined to the mucous membrane, glands in the wall for as long as a year. There are three methods of spread: (a) direct infiltration, (b) by the lymph vessels, and (c) by the blood stream.

(a) *Spread by Direct Infiltration*. Tumours situated at the pelvic rectal junction encircle the wall of the rectum producing stenosis. At a late stage they spread through the rectal wall and reach the parietal peritoneum, where they may give rise to secondary nodules, or spread to adjacent viscera such as the bladder, the ureters, or the uterus.

A carcinoma in the ampulla grows centrifugally, especially when of the crateriform ulcer type. Occasionally nodules appear at a distance from the parent tumour, presumably the result of localized spread in the submucous lymph channels.

The muscular coats are penetrated first at the central or oldest part of the tumour, and the growth then spreads in the fat and areolar tissue around the rectum. At this stage it lies within the fascia propria of the rectum, and not infrequently extends in this plane for a considerable distance without involvement of adjacent organs, or even of the regional lymph glands. Later, when the fascial covering is invaded and the pararectal tissues are invaded the rectum may become a type of recto-

fixed to the sacrum or to neighbouring viscera. By direct spread the base of the bladder, the seminal vesicles, or the prostate may be involved, and in the final stages fistulæ may develop. In women the posterior vaginal wall is often implicated. Occasionally abscess formation occurs in the pelvic cellular tissue or in the ischio-rectal fat, from leakage at the site of the tumour.

(b) *Spread by the Lymph Vessels* Examination of specimens removed at operation shows that the regional lymph glands are the seat of metastasis in about 50% of cases. Usually only a few glands are affected, but sometimes, and especially in rapidly growing tumours (even at an early stage), there may be very widespread involvement. In the majority of cases the glands are unaffected until the tumour has penetrated the muscular wall of the rectum. Enlargement of the glands from infection is common and greater than usually occurs from metastasis.

The glands are situated in the perirectal fat and within the fascial sheath, and are disposed around the lower part of the superior hæmorrhoidal artery and its terminal branches, and when the rectum is removed (enclosed in its sheath) the glands are included. The affected glands are found usually a short distance above the level of the tumour, but in a few instances, those at a higher level may be the site of metastasis without involvement of those adjacent to the tumour, but metastasis in glands higher than the main trunk of the superior hæmorrhoidal artery is exceptional. In the radical operation for carcinoma of the rectum removal of the higher glands should be ensured by ligation of the superior hæmorrhoidal artery at as high a level as possible.

Spread of carcinoma beyond the rectum by a general lymph vascular permeation appears to be prevented by the investing fascial sheath, therefore, involvement of the peritoneum, the levator muscles, and the anal sphincters is very rare. This justifies a fairly circumscribed removal.

As in carcinoma of the breast, so in carcinoma of the rectum, the presence of glandular metastases has an important relationship to the probability of local or general recurrence after operation. Thus Gabriel found that there was a 19% survival after three years, in cases in which metastasis had been demonstrated, as compared with 86% in cases in which the carcinoma was confined to the walls of the rectum and in



FIG. 24. Cauliflower type of carcinoma of rectum.

(Department of Surgery, University of Edinburgh)

which there was no metastasis. Even in cases with extra rectal spread and without metastasis the survival rate (over the same period) was 73% which signifies that glandular metastasis is more important in prognosis than the extent of the tumour.

(c) *Spread by the blood stream* is infrequent but is not necessarily a late feature of the disease. It occurs most frequently in rapidly growing tumours in young subjects. Generally the liver is involved alone but in rare instances metastases are found in the lungs and other organs. When recurrence takes place after operation the liver is usually affected. Prior to radical operation the liver should be examined because thereby a needlessly severe operation may be avoided.

Carcinoma of the rectum is often latent until an advanced stage of



FIG. 246. Cancer of the rectum. The tumour is an adeno-carcinoma composed of columnar cells arranged in fairly well formed acini.

the disease and until ulceration of the tumour occurs symptoms are frequently absent. Pain is a late feature but ultimately it may give rise to great distress. Ulceration results in abundant mucous discharge and bleeding and sometimes hæmorrhage is very profuse and even fatal. When the growth is placed high in the rectum obstruction of the colon results and may be acute. Death has occurred from perforation of a rectal carcinoma into the peritoneal cavity but it is a rare complication. Involvement of the pelvic nerve trunks may occur at a late stage.

### CARCINOMA OF THE ANUS

Cancer at the anus generally arises at the junction of the columnar and squamous cell lining. Usually there is no obvious pre-cancerous lesion but occasionally it is preceded by a fissure, an ulcer or a burn.

The tumour is a squamous cell carcinoma, it may be papillary in type or a crateriform ulcer. It does not tend to spread up the rectum, but it may invade the skin of the perineum extensively. Involvement of the anal sphincter may lead to incontinence. Metastatic growths develop in the inguinal lymph glands. In many instances the disease is first seen when successful treatment is impossible.

### MELANOMA OF THE RECTUM

This type of tumour is of rare occurrence. It arises from the skin within the anal canal as a hard nodular mass dark in colour. It tends to grow upwards into the rectum, the coats of which may be extensively invaded. There is variation in its degree of malignancy: some tumours remain localized and grow only slowly, others grow rapidly and metastasize widely both to the lymph glands and by the blood stream. The inguinal glands are sometimes the seat of secondary deposits. Pigmentation of the regional glands may be due simply to phagocytosis of pigment granules, but is more often due to cellular metastases.

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## CHAPTER XXVI

### DISEASES OF THE VERMIFORM APPENDIX

#### APPENDICITIS

THE history of appendicitis requires no recital, for almost in its entirety it comes within living memory. Until 1885 the disease was rare, yet within twenty years it had attained the position of being the most common of all acute abdominal illnesses. At first consideration it might be supposed that such a remarkable change in incidence, occurring at the time when the surgery of the abdomen was advancing most quickly, might be attributable principally or entirely to a keener recognition of the disease, but, as Rendle Short has shown, this is not so—the increase is actual, not merely apparent.

Although appendicitis was known in the eighteenth century, it received little recognition until 1886, when Fitz described a long series of cases, distinguished it clearly as the commonest cause of "perityphlitis," and gave it the name now universally adopted. From 1886 to 1905 there was a great increase in the frequency of the disease, first noticeable in the cities and towns of Great Britain and America, and later in the country districts, since 1905 the incidence has remained unchanged.

Appendicitis is almost entirely a disease of the Western world, and particularly of Great Britain and America. In Denmark, Spain and Italy it is still uncommon, in the rural districts of Rumania and other parts of Eastern Europe it is distinctly rare, and amongst the native populations of many parts of Asia and Africa it is almost unknown. In general, the disease is one of modern civilized life, although a few civilized races *e.g.* the Japanese, remain free from it. There is ample evidence that its incidence does not depend upon any racial, climatic or geological factors, but is intimately related to modern developments in the diet or mode of life of the Western world. When natives of the East adopt the dietary of Great Britain or America they become liable to appendicitis, but Europeans living in the East do not lose their susceptibility, for they retain their Western customs. In the United States of America the coloured people in country districts of the south maintain their traditional ways of living, and remain free from appendicitis, but those who migrate to the cities or northward and adopt the habits of the whites lose this immunity.

There is evidence that the increased frequency of appendicitis is associated with the more general use of a diet rich in proteins. In Great Britain and America the period 1885–1905 was one of greatly increased prosperity for the industrial classes, and a correspondingly greater demand for an animal diet, moreover, a close correspondence between meat eating and appendicitis is indicated by the rarity of the disease in communities where the diet is principally vegetarian, as in



the rural districts of Eastern Europe and Asia, and in the poorhouses, prisons and asylums of this country. But the consumption of proteins cannot be the only factor, for meat eating was indulged in before 1880, as Rendle Short has pointed out, the "Roast Beef of Old England" has been appreciated for centuries, and, indeed, from contemporary accounts, too well! Constipation might be regarded as a predisposing factor, but, as Pepys bears witness, also is no modern development. According to Rendle Short, the essential difference between our food and that of our forebears lies in the relative paucity of cellulose and in the consequent diminution in the bulk of the excreta, and it is possible that this, in conjunction with a high protein content of the diet, is responsible for the increased frequency of appendicitis, the protein excess permitting increased putrefaction in the lower bowel, and the lack of cellulose leading to inspissation of the appendicular content.

Experimentally, Wilkie demonstrated in cats the important relationship of a protein diet to infections in the lower bowel. The cat has no appendix, but an isolated portion of the lower ileum may be fashioned to represent one. If this "artificial appendix"

be abstracted, by ligation of its proximal end, the morbid changes that follow depend partly upon the nature of the animal's diet. If the diet has been entirely carbohydrate for a long period, the pathological changes develop slowly and the cat may survive several days, but an animal on a meat diet may die within twenty-four hours.

**Ætiology of Appendicitis.** Apart from the question of diet, which has already been considered, there are three important factors in the ætiology of appendicitis, (1) the structure of the appendix, (2) its contents, and (3) its shape.

(1) *Structure.* Lymphoid tissue abounds in the wall of the appendix, where it forms dense follicles in the mucous and submucous coats. It appears in quantity shortly after birth, it is most abundant in childhood and adolescence, and after the age of thirty it tends, like lymphoid tissue elsewhere, to atrophy. It probably constitutes a barrier against infection, which, as elsewhere, may be overcome if the bacterial attack is overwhelming.

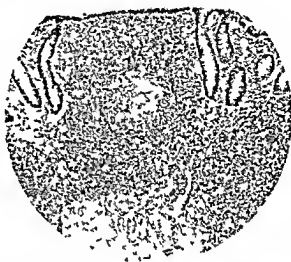


FIG. 247 Section of the appendix (low power) showing a large lymph follicle situated immediately deep to the epithelium of the mucous membrane (Laboratory of Royal College of Physicians of Edinburgh)

forces of the body, the particular "type" of affection in any individual is merely the resultant of these two processes. Appendicular disease should be studied as a continuous story rather than in serial form.

The severity of the disease is greatly modified and aggravated by obstruction of the appendicular lumen. If the appendix remains unobstructed in an inflammatory attack, the disease usually pursues a mild course, but when the lumen is occluded any pre-existing or potential infection is intensified, for inflammatory products remain pent up and gangrene or perforation may rapidly supervene.

**Appendicitis without Appendicular Obstruction** The organisms

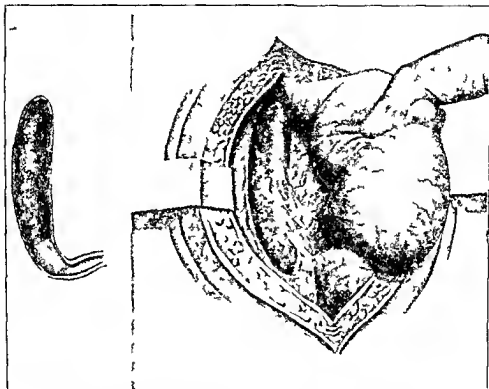


FIG. 218. Acute appendicular obstruction due to impaction of a concretion at the point at which the retrocaecal appendix is kinked. The appendix distal to the obstruction is distended and gangrenous.

(Department of Surgery, University of Edinburgh.)

principally concerned in appendicitis are colon bacilli, streptococci, and anaerobic organisms. Generally they are derived from the lumen of the large bowel, infecting the appendix *via* its lymphoid tissue, it has been suggested that some organisms, particularly streptococci, may reach the appendix through the blood stream from some distant focus.

The disease commences in the lymphoid follicles of the mucosa, it may remain limited to this membrane—*catharrhal appendicitis*—but almost invariably it spreads to involve the other coats. The mucous membrane becomes thick, oedematous and congested. Hemorrhagic spots and small erosions appear on its surface and the whole appendix becomes swollen and turgid. With further extension of the infection

the serous surface becomes covered with fibrinous exudate, and local mild peritonitis develops. The disease usually does not progress acutely, but occasionally, particularly where a concretion or other foreign body causes pressure upon the diseased wall, a perforation or a peri appendicular abscess may occur. At any part of the course, moreover, the lumen of the appendix may become occluded by swelling of the mucosa, and with the onset of an obstructive element graver developments take place. If uncomplicated, the disease may subside, but complete resolution, with return to the *status quo ante*, is uncommon, infection is likely to recur, often with enhanced severity, and inflammatory scarring may lead to stricture and subsequently to an obstructive lesion.

**Appendicitis with Appendicular Obstruction.** This is a considerably more dangerous type of disease, and forms a large proportion of the cases seen at operation. In its pathology it resembles one form of acute intestinal obstruction, for the appendix becomes a closed loop of bowel containing septic faecal matter.

The effects of acute appendicular obstruction depend upon the infective nature of the matter in its lumen and also upon the presence of much organic faecal matter which may readily putrefy. If infection is mild the appendix becomes thickened, and gradually distends with mucopurulent fluid to form a *mucocoele*, one variety of chronic appendicitis (*q.v.*). If the infection is of greater degree the appendix becomes distended with pus—*empyema of the appendix*—and later may become gangrenous and perforate. If the infection is highly virulent and the appendix contains much faecal matter, gangrene and perforation may occur with extreme rapidity, causing widespread peritonitis—*fulminating appendicitis*.

*Perforation of the appendix* through a gangrenous spot is an important event in the progress of the disease, for if the appendix has previously been distended the grossly infected contents are forced out and will contaminate surrounding tissues. In rapidly progressive cases perforation may occur within a few hours of the onset of the attack, and may lead to widespread peritonitis, or, if the appendix is surrounded by adhesions a local abscess may result.

*Changes around the Appendix.* These depend upon the intensity and virulence of the infection and upon the existence of adhesions that may limit the spread of the disease.

If the infection is rapid and virulent, as when the appendix perforates quickly, or when a slowly forming abscess suddenly bursts its protective wall, a widespread peritoneal infection ensues. The peritonitis commences first around the appendix and over the pelvic organs and pelvic coils of ileum, later it spreads into the upper part of the abdomen. If resistance is great, the peritoneal exudate becomes thicker, and adhesion of opposed serous surfaces leads to loculation of the pus. In these cases intestinal obstruction is a common and grave complication.

Should the infection spread more slowly, it excites a vigorous reaction on the part of surrounding tissues and a dense protective barrier forms against further extension of the disease. A lymphic exudate is poured

out, containing many pus cells but few or no organisms. The serous surfaces become ingested and adhere, the great omentum envelops the appendix like a thick mantle, and neighbouring coils of intestine become immobilized to form a barrier around the infective focus.

At this stage the infection may subside, leaving a large inflammatory mass, perhaps the size of an egg, which slowly diminishes. In the course of time many of the adhesions resolve, and the appendix may become shrivelled and fibrotic, though relapse of infection is common.

**Appendicular Abscess.** If the disease progresses, though limited by the protective barrier there develops a localized abscess containing thick foul smelling pus. The abscess may be small, buried in a mass of adhesions, or it may attain considerable size, displacing the neighbouring intestines as it grows. If untreated it may open into one of the hollow organs, the cæcum, rectum or bladder, or it may eventually reach the skin surface, occasionally, however, it bursts into the general peritoneal cavity and causes widespread, rapidly fatal peritonitis. The situation of the abscess depends upon the position of the appendix. Most often it is in the right iliac fossa just medial to the anterior superior spine, not infrequently it is in the pelvis, or behind and lateral to the cæcum, but it may be in the region of the gall bladder, in the mid line below the umbilicus, or even on the left side.

**Appendicitis due to Parasites.** *Threadworms* (*oxyuris vermicularis*) are of particular interest as a cause of appendicitis. They are rarely responsible for acute or fulminating inflammations, but are not uncommon, particularly in children, in association with mild recurring attacks. The parasites are usually multiple, and often collected in a small clump close to the base of the appendix which may contain a little purplish or prune coloured fluid. Female parasites are more common than male and are often heavily laden with ova, and Still has suggested that they use the appendix as a breeding place. It might be supposed that threadworms would predispose to appendicitis merely as irritating foreign bodies, but it has been shown that there is an actual invasion of the mucosa by the worms, which in serial sections of the appendix can be seen lying deep in the wall and even penetrating as far as the muscular coat. In this way they produce minute ulcerations and hemorrhages which readily predispose to infection. Threadworms give rise to recurring mild attacks in which the predominating feature is the occurrence of colicky pain diffused over the abdomen with little pain or tenderness on pressure over the appendix. Occasionally the attacks are febrile and the temperature may even mount to 102°—103° F.

A round worm (*ascaris lumbricoides*) may enter the lumen of the appendix and lead to appendicular colic or mild appendicitis. The worm occupies the whole lumen of the appendix. If its presence be unrecognized, subsequent histological examination of the transversely sectioned appendix will reveal a remarkable appearance as of a double barrelled tube, each barrel lined by intestinal mucous membrane, the outer one formed by the appendix, the inner by the gut of the parasite.

**Cause of Pain in Acute Appendicitis.** The cause of the pain in acute appendicitis forms a subject of great interest in relation to the general physiological aspects of abdominal pain. The appendix, like other viscera, is but little sensitive to ordinary stimuli, and when the abdomen is opened under local anæsthesia it may be handled without discomfort, yet the pain of acute appendicular disease may be intense.

One of the first important studies of abdominal pain was made by Ross in 1857. He formulated the hypothesis that visceral disease may give rise to two varieties of discomfort, namely, true splanchnic pain felt in the viscus itself, and somatic or referred pain felt in the parietes. The existence of splanchnic pain was denied by Mackenzie, who held that all abdominal pain is somatic, *i.e.*, referred to the parietes. In a number of papers which appeared from 1892 to 1906 Mackenzie put forward the theory that pain of visceral disease results from a "viscero-sensory reflex" action. Impulses extend from a viscus along its afferent autonomic fibres to the spinal cord and though these impulses are themselves unperceived by the brain they give rise to painful sensations by overflowing to neighbouring parts of the cord and irritating adjacent sensory nerves. According to this view, impulses from the appendix reach the eleventh or twelfth thoracic segments of the cord and "overflow" to sensory nerves at this level, so that they are appreciated by the brain as impulses originating in the lower abdominal wall. Similarly the hyperæsthesia associated with some abdominal diseases could be regarded as due to over-excitability of the sensory nerves of the parietes, and muscular rigidity could be regarded as resulting from 'overflow' stimulation of motor nerves (visceromotor reflex).

Mackenzie's conception, however, fails to explain many aspects of abdominal pain, and there are fundamental objections to the whole theory of viscerosensory and visceromotor reflexes. The evidence against these views, exemplified in a study of the pain of acute appendicitis has been discussed by Morley. He points out that there can be no doubt, as Hurst has shown, that true splanchnic pain does exist. Painful stimuli can originate in hollow viscera either from spasm or increase of tension of the muscle fibres. When the stimuli arise in any portion of the mid-gut (which includes the appendix) such pains, whether colicky from peristalsis or continuous from distension have two characteristic features, (1) since the visceral nerve supply is not strictly localized the pains are ill-defined, and (2) since developmentally the mid-gut is a median organ, the pains are felt principally near the mid line.

Kinsella has recently supported these views as a result of direct observations made during the performance of appendicectomy under local anæsthesia. He has shown that whereas the appendix, like other viscera, is insensitive to localized injury, *e.g.*, by crushing with a forceps, considerable pain is caused by squeezing the whole organ between the fingers. Such pain is almost always referred to the midline in the umbilical region.

It is a matter of everyday observation that in acute appendicitis there are usually two distinct varieties of pain. In early stages of the

attack the pain is ill defined, and principally felt close to the mid line, around the umbilicus or in the epigastrium. It is obvious that this initial pain of acute appendicitis has the characteristics of true splanchnic pain, it may be colicky from excessive peristalsis or continuous from increased intra appendiceal tension. Early colicky pain in acute appendicitis invariably indicates an obstructive lesion.

The later variety of pain in appendicitis, which usually becomes evident a few hours after the onset of an attack, is entirely different in situation and character from its forerunner. It is strictly localized, usually in the right lower quadrant of the abdomen, it is continuous, never colicky, and it is intensified on palpation or by any sudden movement. The mechanism of this later pain cannot be attributed to a viscerosensory reflex, for the median development of the appendix and mid gut would postulate a bilateral innervation and bilateral pain. Moreover, on the reflex theory the innervation would be quite independent of the final position of the appendix, which migrates to the right side at a late period in development, yet it is a common experience that the localized pain of appendicitis begins directly over the diseased organ, and indeed is a reliable guide to its situation. This would seem to indicate that the pain is not dependent upon any reflex mechanism but is due to irritation of sensitive structures related to the appendix.

It is well known that the anterior parietal peritoneum is exquisitely sensitive, and in many cases the local pain of appendicitis is due to irritation of this membrane. The parietal peritoneum lateral to the cæcum is also very sensitive, the posterior peritoneum less so. Kinsella has shown also that the meso appendix, like the mesentery of the small intestine, is extremely sensitive and such procedures as clamping or ligating the meso appendix are productive of great pain.

*Muscular rigidity*, a very constant feature of appendicitis, is to be regarded as a protective mechanism of great value, for it immobilizes the abdominal wall over the site of infection and thus assists in limiting the spread of the disease. According to Mackenzie's hypothesis, the rigidity is due to the radiation of impulses from afferent autonomic filaments to the anterior horn cells of the spinal cord—a visceromotor reflex—but the same considerations hold good that have been referred to in connexion with abdominal pain, and there can be no doubt that, like pain, the rigidity is due directly to irritation of the parietal peritoneum. It is for this reason that the rigidity from a retrocæcal appendix is most severe towards the loin whilst that from an appendix overhanging the pelvic brim is situated just above the pubis.

*Cutaneous hyperæsthesia*, a somewhat inconstant sign in acute appendicitis, can also be attributed only to irritation of the parietal peritoneum.

It has been stated that hyperæsthesia is present in appendicitis only when the appendix is unruptured, but this does not accord with general experience. Often it appears as though the degree of hyperæsthesia depends upon the proximity of the appendix to the parietes, the most intense hyperæsthesia being associated with an appendix that lies immediately under the anterior abdominal wall.

## RECURRENT AND CHRONIC APPENDICITIS

It is well known that acute appendicitis, particularly, in its less acute forms is very apt to recur, and indeed in the great majority of cases seen in hospital there is a history of several previous attacks with intervening periods of good health. Less often the history is of minor or transient spasms of pain in the lower abdomen recurring frequently during a period of weeks or months. Generally in such circumstances there has been a foreign body such as a fecal concretion in the appendix which by impacting has given rise to attacks of colic and ultimately to acute obstructive appendicitis.

Foreign bodies in the appendix may occur in a healthy appendix or in one which from kinking or stenosis is unable to empty itself properly. The foreign body is usually a fecal concretion but a great variety of other objects have occasionally been found. Reference has already been made to the occurrence of thread worms and occasionally round worms, and in children the former are not infrequently the cause of mild appendicular discomfort. A striking instance of a symptom-producing foreign body is seen when lead pellets, such as may be swallowed with shot game, find their way into the appendix. Occasionally as many as forty or fifty pellets may collect in the appendix, eventually becoming coated with inspissated fecal matter and either faceted like gallstones or glued in a single mass. They give rise to symptoms either by virtue of their weight, or by irritating intermittent appendicular spasms with pain referred to the umbilical region.

Chronic appendicitis was formerly regarded as a common disease and has been held responsible for numerous symptoms or signs including pain in the lower abdomen indigestion flatulent dyspepsia, anorexia, nausea and vomiting. Experience has shown, however, that in such circumstances the appendix

commonly shows no naked-eye evidence of disease, or perhaps is fibrotic or atrophied, while the results of operation are generally disappointing. For these reasons it is now agreed that true chronic appendicitis is a somewhat rare disease. In such cases as do occur the primary feature is usually a chronic obstruction of the appendix.

Chronic Obstructive Appendicitis may result from previous acute disease, or from narrowing of the lumen due to any other cause. If the obstruction remains partial, the fecal content becomes inspissated



FIG. 249 Maxillary of appendix with diverticula, due to progressive narrowing of the lumen at the proximal end of the appendix by fibrosis. The diverticula project into the meso-appendix and are surrounded by adherent fibro-fatty tissue.

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sated, and the mobility of the appendix is deranged. If the obstruction slowly becomes complete a *mucocoele* may develop. Sometimes the mucous membrane herniates through weak places in the muscular coat, particularly at those points on the mesenteric attachment where the vessels enter, and one or more *diverticula* result. Rupture of a mucocoele or of a diverticulum into the peritoneal cavity may give rise to a curious mucoid change known as *pseudo myxoma peritonei*, in which large masses of jelly like mucoid material collect in the peritoneal cavity. The condition is similar to that following rupture of a pseudo mucinous cyst of the ovary and appears to be due to the engrafting of mucus secreting cells upon adjacent peritoneal surfaces, but such cells can rarely be satisfactorily demonstrated. (See also p 548.)

### TUMOURS OF THE APPENDIX

Two distinct types of tumours occur in the appendix the one—adenocarcinoma—extremely rare the other—carcinoid tumour—quite common. A pedunculated adenoma is present occasionally and may cause intussusception.

**Adeno-carcinoma.** Adeno carcinoma is a rare tumour. It occurs



FIG 253 Carcinoid tumour of the appendix  $\times 110$ . The tumour is composed of spheroidal cells arranged in alveoli. Note the close relation of the cells to the muscle fibres at the lower part of the section.

(Laboratory of Royal College of Physicians of Edinburgh.)

in elderly subjects and resembles adenocarcinoma in other parts of the bowel. It is composed of columnar cells derived from the mucous membrane arranged in acinar formation and supported by a connective tissue stroma. It tends to ulcerate at an early age and to infiltrate neighbouring parts and may metastasize to the liver or to more distant sites.



**Carcinoid Tumour** A carcinoid tumour is considerably more common and is said to constitute 0.4% of all appendiceal lesions found at operation. It occurs commonly in young persons, especially between the ages of twenty and thirty years, and is of particular interest in several respects, for although locally invasive and possessed of certain of the microscopic features of carcinoma it does not spread beyond the appendix and only seldom metastasizes.

A carcinoid tumour may occur in any part of the appendix, and is especially common near the tip. Rarely two or three such tumours coexist. The tumour forms a hard, rounded, circumscribed nodule, usually small and rarely exceeding the size of an almond, and it may be recognized on naked eye examination by its characteristic golden yellow colour.

When small the tumour lies in the substance of the appendix wall, and the mucous membrane over it is intact. When larger it projects under the serous surface and it may press upon and thus occlude the lumen. Occasionally a tumour at the base of the appendix has determined the onset of appendicular obstruction and acute appendicitis. In some cases when the appendix is shrivelled and its lumen obliterated by fibrosis the tumour assumes a central position.

*Microscopically* a carcinoid tumour is composed of solid masses of epithelial cells arranged in alveoli and supported by a stroma of connective tissue (see Fig 250). Most of the cells are of spheroidal shape with a central rounded nucleus and a finely reticulate protoplasm. In places the cells are columnar in shape, and arranged in palisade fashion. Yet again there are sometimes long, bulbous headed racket shaped cells, which may be arranged in rosettes. Many of the cells contain cholesterol esters and other lipoids, and these are responsible for the golden yellow colour characteristic of the tumour. Other cells contain fine chromatin granules with a specific affinity for silver stains (argentaflin cells).

The tumour at first lies embedded in the muscle coat, and it spreads between the muscle bundles without destroying them. Often the tumour cells appear to be closely related to the nerve fibres of the mesenteric plexus (Auerbach).

*Origin of the tumour* Formerly the tumour was regarded as either a true carcinoma of low grade malignancy or a basal-cell carcinoma derived from the mucous membrane, but these views are now generally discarded, and at present the theories most widely held are those of Ehrlich and of Masson. Ehrlich was impressed by the close relationship of the tumour cells to the nerve fibres of Auerbach's plexus, and on the basis of this observation and of the microscopical appearance of the cells he regarded the tumour as a neurocytoma originating in the autonomic nerves. Masson has examined the microscopic characters of the cells in great detail, and he has brought evidence to show that they are derived from the so-called Kulchitsky cells of the crypts of Lieberkuhn. These cells are believed to be of entodermal origin, but to be related intimately with the autonomic nervous system, and they are characterized by a specific affinity for certain silver stains. On the basis of his observations Masson has called the tumours *argentaflin*

*tumours*, and has classed them correspondingly with tumours of the adrenal medulla and of the paraganglia of the autonomic nervous system.

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## CHAPTER XXVII

### DISEASES OF THE PERITONEUM

THE peritoneal cavity, with its various recesses and compartments, forms a potential space of vast dimension. The lining membrane is composed of a single layer of flat endothelial cells supported by delicate areolar tissue. It forms a smooth glistening surface, admirably adapted to subserve its principal function of facilitating the physiological movements of the gut and viscera.

The intimate relation of the peritoneum to the alimentary tract and pelvic organs renders it peculiarly liable to implication in diseases originating in these parts but fortunately, in addition to its physiological role as a gliding surface, the peritoneum has valuable properties for combating even gross infection. Indeed the peritoneum can deal effectively with massive doses of organisms which in most other tissues would spread widely. From the time of the advent of organisms to the gut of the new born child the peritoneum is continually subject to small bacterial assaults and thus acquires an increasing natural resistance. By contrast the pleura and pericardium although derived from the same primitive body cavity, are rather less resistant to infection.

**Absorption from the Peritoneal Cavity** Owing to its vast surface and the specialized character of its epithelium, the peritoneum has an immense absorptive power. In health this property is mainly protective for it ensures that small amounts of deleterious substances are rapidly disposed of but in peritonitis the rapid absorption of toxic products constitutes one of the gravest dangers of the disease.

It is now established that the mode of absorption of fluids and soluble toxins differs from that of particles such as bacteria. When fluid is injected into the peritoneal cavity comparatively little reaches the thoracic duct, and the greater part passes directly into the blood stream by a simple physical process of dialysation through the endothelial lining membrane. The rate of absorption is extremely rapid, and in some respects the peritoneum is a speedier avenue for the administration of fluids than the subcutaneous tissue.

Absorption takes place equally readily and rapidly from all parts of the peritoneal cavity. Accordingly the design of the semi sitting (Fowler's) position, namely, to divert the toxic products to a "non-absorptive" region of the peritoneal cavity, can no longer be upheld. It has too the added disadvantage of favouring venous stagnation in the lower part of the body, and of cramping respiratory movement. There is evidence, too that it increases the tendency to subphrenic abscess (see p. 546).

The routes of removal of particles such as bacteria may be demonstrated experimentally by the injection of such substances as Indian ink or colloidal silver. After injection into any part of the cavity such

pigment is rapidly collected in two clearly defined regions, namely, over the greater omentum and in the subphrenic region Paterson Brown showed that the route of absorption from these regions varies in different animals. In rabbits the pigment rapidly reaches the thoracic duct, but in cats and dogs the thoracic duct is hardly affected at all, and the main route of transference is along the lymph vessels of the retrosternal region by which it reaches the cervical veins. There is accumulated evidence that in man the routes are similar and that the thoracic duct plays little part in peritoneal drainage.

**Response of the Peritoneum to Infection** When organisms reach the peritoneal cavity they evoke a vigorous reaction. Hyperemia is excited, fluid rapidly exudes from the peritoneal surfaces, and leucocytes and endothelial cells migrate into the cavity, so that the infecting agents are first diluted and dispersed and then subjected to phagocytosis. At first the exudate is turbid and watery, and in some types of infection remains thin, or is sometimes blood stained, but usually it becomes thick and purulent in the later stages of the disease.

If infection occurs acutely, the peritonitis rapidly becomes wide spread, but if the onset is slow the inflammatory process soon becomes delimited and walled off by fibrinous adhesions.

The process by which infection becomes circumscribed affords a remarkable illustration of nature's defensive mechanism, for it depends partly on local inflammatory changes in the peritoneum, partly upon a curious attribute of the omentum, and partly upon simultaneous immobilization of the viscera and abdominal wall. The peritoneal surfaces around the infected region lose their glossy appearance, and adjacent coils of intestine adhere to the abdominal wall, the omentum is disposed around the focus of disease, intestinal peristalsis is inhibited reflexly or by toxic paralysis of the muscular coats, the movements of the abdominal wall are reduced by reflex muscular spasm, and thus by this mechanism of immobilization the defensive processes are perfected. The most remarkable part of this process is the striking protective behaviour of the omentum, which has earned for itself the title "the policeman of the abdomen". No matter where the focus of infection lies, whether in the gall bladder or the uterine tube, the omentum, if given time, will become adherent to it and envelop it. There is, of course, no purposeful movement on the part of the omentum, and the whole process appears to depend on the abdominal movements, peristaltic and respiratory, and also on the fact that the inflamed peritoneum favours cohesion.

**Peritoneal Watersheds** The irregular contour of the posterior abdominal wall and the complicated arrangement of the peritoneal folds create barriers which limit the diffusion of septic fluids and promote the localization of peritoneal infections.

The peritoneal cavity may be regarded as having two compartments, the pelvic portion and the abdomen proper. The latter is naturally subdivided into upper and lower compartments by the transverse colon and its mesocolon. These two compartments communicate in front of the omentum. The upper compartment lies above and in front of the omentum and mesocolon, and contains three common sources

of peritoneal inflammation, the stomach, duodenum and gall bladder. The lower compartment lies below and behind the omentum and communicates directly with the pelvis. It contains, in addition to small intestine, the commonest source of infection, the appendix.

The lower compartment of the abdominal cavity is divided into right and left portions by the mesentery of the small intestine, which tends to limit the spread of infection from one side to the other.

In the posterior wall of the abdomen the vertebral bodies form a ridge which, with the root of the mesentery, diverts fluid from the midline towards either flank, where it collects in the paravertebral recesses.

These topographic features have an important effect in directing the spread of extravasations and in circumscribing infections. Thus in a leaking duodenal ulcer, extravasation is deflected mainly alongside the ascending colon towards the pelvis. Even though the patient maintains a recumbent attitude the greatest accumulation is in the pelvis and lower abdomen. In appendicitis fluid exudate at first gathers in the right flank and pelvis and is usually circumscribed by the omentum, the mesentery and coils of the small intestine. When it is in greater bulk it may well up from the pelvis and is diverted mainly to the left due to the oblique fixation of the mesentery. Extension of infection to the subphrenic space is of rare occurrence relative to the frequency of peritonitis and as it develops chiefly as a post-operative complication it is likely that diminished diaphragmatic movement together with the access of air rather than posture allows infection within this normally confined area.

### ACUTE PERITONITIS

Peritonitis like any other inflammation, may be the outcome of bacterial or non bacterial irritation. Non bacterial peritonitis occurs when a sterile foreign substance or an effusion of blood is present in the cavity, and occasionally when a cyst ruptures or when sterile bile is extravasated, but these are rare occurrences, whereas peritonitis from infection is common. Moreover, even the rare non bacterial type does not usually remain aseptic, for the effusion is very liable to secondary infection, especially with organisms of mild pathogenic properties, such as *staphylococcus albus*.

In the majority of cases acute peritonitis is due to infection from some local focus in the abdomen, especially in the alimentary tract, its appendages or the pelvic organs, but occasionally it is a hæmatogenous infection as in septicæmic conditions. Rarely, as in gonococcal peritonitis it seems to follow direct infection from the exterior, by way of the uterine tubes.

The common causes of acute peritonitis include (1) perforation of hollow organs, (2) simple inflammations and (3) strangulation of bowel. Appendicitis heads the list and after it come salpingitis perforations of peptic ulcers cholecystitis, volvulus etc.

The extent and gravity of acute peritonitis depend upon many circumstances, and clinically no two cases are similar. The virulence of the infection varies greatly. In gonococcal salpingitis or in chole-

cystitis it is almost always mild, in appendicitis it may be mild or severe, and in perforative lesions and diseases of the colon it is often fulminating. Staphylococci and non hæmolytic streptococci are often relatively innocuous, and coliform bacilli vary greatly, whereas hæmolytic streptococci and anaerobes are often intensely virulent.

**Bacteriology of Acute Peritonitis.** As may be expected from the diversity of origin of the disease the bacterial flora of peritonitis is very varied. *Bacillus coli* is undoubtedly the commonest, but hæmolytic streptococci are not infrequent, and non hæmolytic streptococci, gonococci, pneumococci, staphylococci or anaerobes occur. In rare cases acute tuberculous peritonitis has been observed. Sometimes there is a mixed infection, especially of coliform bacilli and streptococci. This is demonstrable in direct films made from the peritoneal exudate, but is apt to be missed on culture, for the more delicate streptococci are liable to be outgrown by coliform bacilli.

**Acute Localized Peritonitis.** Unless infection of the peritoneum be very acute it remains localized, and soon becomes circumscribed by adhesion of intestinal loops to the parietes. This often ends in resolution, and the inflammatory products are absorbed, but if the infection is more severe a local abscess may form, either in the neighbourhood of the original infection, e.g., around the appendix, or at some more distant site, such as the pelvic cavity or the subphrenic space. A *pelvic abscess* may follow appendicitis, salpingitis or other inflammation. The abscess may remain small and eventually undergo resolution, or it may enlarge and perforate into the rectum or other hollow viscus, or even point externally. If unrelieved, the abscess may burst into the general peritoneal cavity.

**Acute Diffuse Peritonitis.** "Generalized" peritonitis is rare, because death usually occurs before this stage is reached. It is more accurate, therefore, to use the term "diffuse peritonitis," which indicates a non circumscribed, and spreading, but not universal, inflammation.

The pathology of peritonitis is essentially the same as inflammation in any other tissue, but its progress is greatly modified and aggravated by two factors peculiar to the situation, namely (1) the *vast extent of the absorptive area, which leads to rapid dispersion of toxins*, and (2) *secondary intestinal paralysis, which brings the danger of obstruction*.

The inflamed peritoneal surfaces become injected, engorged and of deep red colour, and the natural lustre is replaced by a dull, matt, velvety appearance. The intestine is dilated and paralysed, and adjacent loops adhere. Often there are masses of thick yellow lymph on the surfaces and in the fluid.

The exudate varies with the type of infection and with its stage. In *B. coli* peritonitis the exudate is usually purulent, yellow or yellowish-white, and with a characteristic fetor; in streptococcal infections it is often thin, turbid, or sanguineous, in mixed infections, especially when derived from the colon, it may have a stercoraceous appearance and smell, and gas may be present. After perforation of a gastric or of a duodenal ulcer the exudate may be mixed with gastric contents or bile, and in strangulation it may be deeply stained with blood.

Willie showed that the microscopic appearance of a diffuse exudate, in addition to demonstrating the type of organisms, may afford a valuable indication of the progress of the infection and consequently of the prospects of recovery. At an early stage the fluid naturally contains many organisms as well as pus cells, but after the peritonitis has progressed for several hours the altered appearances suggest its extent and the degree of reaction. In a virulent infection the fluid still contains many free organisms, and the pus cells show signs of degeneration. If the resistance is good, however, most of the organisms will have undergone phagocytosis. In later stages of a resolving peritonitis the striking feature is the presence of many large mononuclear or endothelial cells, which appear to act as scavengers both of bacteria and of damaged polymorphs.

*The stage of resolution of peritonitis* affords evidence of the remarkable properties of the endothelial lining membrane of the peritoneum. Fluid exudate is rapidly absorbed, and even large masses of fibrinous exudate quickly disappear. In most cases adhesions are absorbed and in a few months there may be little sign that there has been peritonitis. In other cases, however, such complete resolution does not take place, and widespread adhesions or long fibrous bands remain, often to cause later trouble from intestinal obstruction. There seems to be an individual idiosyncrasy towards the formation of adhesions.

**Cause of Death in Peritonitis.** The cause of death in peritonitis is not fully understood. Septicæmia rarely plays a part, but it is not certain whether the profound toxæmia that is so characteristic a feature is due wholly to absorption of toxins from the peritoneal cavity or to secondary intestinal obstruction (*see also* p. 497). The question is of great importance from the therapeutic point of view, for the treatment of peritonitis necessitates rest, whereas the treatment of partial intestinal obstruction demands maintenance of peristalsis.

Bonney and Sampson Handley supported the view that intestinal obstruction is an important factor. It is supposed that in diffuse peritonitis the whole intestine is paralysed—paralytic ileus—but Handley believes that this is unlikely and that only those parts of the gut lying in the pelvis are, in the first instance, involved. He pointed out that at the time of death peritonitis rarely reaches the level of the umbilicus and that the jejunum is comparatively unaffected, whereas the ileum, which lies bathed in pus in the pelvis, is completely flaccid. According to this view, there is often a double obstruction—ileus duplex—namely, in the ileum and in the pelvic colon, and the rational treatment consists in diverting the jejunal contents into the colon, and in draining the large gut at the cæcum.

Experience has not confirmed these views. In diffuse peritonitis there is, undoubtedly, a toxic paralysis of the intestinal muscle, but it seems probable that its effect is mainly protective, in that it inhibits intestinal movements and circumscribes the infection. It seems probable that the essential factor in death from peritonitis is the absorption of poisonous products from the infective area, and that the obstruction factor is of somewhat secondary importance.

Paralytic ileus must be clearly distinguished from another quite

distinct complication of peritonitis, namely, a mechanical obstruction due to plastic adhesions between intestinal coils. Such adhesions are often formed at a stage when the toxæmia of peritonitis has been overcome, and thus the patient after recovering from peritonitis may be a victim of obstruction.

### PERITONEAL ADHESIONS

Many so called adhesions are really congenital folds of peritoneum. True pathological adhesions may follow any type of acute or chronic infective process within the abdomen and are common also after operative intervention in this region.

Under any such circumstances at first there is a more or less extensive cohesion between the inflamed surfaces as a result of which the viscera are bound closely to one another or the parietes. Under the influence of the visceral movements, in the course of time some of these adhesions stretch and at the same time become more narrow to form sheets or isolated bands, which by kinking or ensnaring loops of intestine, or by initiating volvulus, may lead to intestinal obstruction.

Complete resolution with disappearance of adhesions may occur even after quite considerable degrees of peritonitis. This is well seen when an appendix abscess is allowed to settle under conservative treatment, for in such circumstances at operation a few months later it is commonly observed that complete restoration to normal has taken place. This is, however, not invariable, and it is generally thought that individual susceptibility plays an important part. The great tendency for adhesions to recur after they have been divided at operation lends to support this view.

Abdominal tuberculosis may cause dense and widespread adhesions. This is most likely to occur after tuberculous infection of the peritoneum, though not infrequently a dense but isolated adhesion is found in the vicinity of a tuberculous mesenteric gland.

Post-operative adhesions often are both dense and widespread. They commonly involve the omentum, which attaches itself to the deep surface of the abdominal wall, and they may also implicate the small and large intestine. Sometimes, doubtless, they are due to wound infection, or to faulty closure of the parietal peritoneum. It has recently been suggested, however, that the presence in the wound of talc derived from the surgeon's gloves may be a factor of importance.

**Talc Granuloma.** Talc (magnesium silicate), when embedded in the tissues or set free in the peritoneal cavity gives rise to a vigorous foreign body reaction with the production of giant cells and much scar tissue. Recent observations show that dense adhesions may develop in as short a time as two weeks. In some cases, talc in the peritoneal cavity has gravitated to the pelvis and led to scarring with obstruction of the Fallopian tubes.

### GONOCOCCAL PERITONITIS

This disease is limited to females. It usually arises within a short time of the primary infection, and is secondary to disease of the Fallo-



pian tubes. In most cases, no doubt, the organisms gain access to the peritoneal cavity by way of the abdominal ostium, in others where this orifice is closed by adhesions or fibrosis it is presumed that infection has leaked through the diseased wall of the tube. Though commonest in adult women, gonococcal peritonitis may affect young girls following vulvo vaginitis.

Infection is usually limited to the pelvis and is most intense around the tubes and ovaries, but occasionally is more generalized. At first there is often an acute phase, but the infection is never virulent and in the course of a few days tends to subside, but it nearly always leaves behind a low grade inflammatory process, which may persist for a long period or never resolve. In the early stages there is an effusion of fluid at first thin and serous, later purulent, and the surfaces of the pelvic peritoneum are congested and covered with fibrinous deposits. Detection of gonococci in the fluid is difficult, and by ordinary cultural methods the fluid usually proves sterile. Usually there is a mixed infection and the presence of gonococci is masked by other organisms, of which the most frequent is a streptococcus.

In the later stages of gonococcal peritonitis the most striking pathological feature is the presence of numerous adhesions, and this is the principal factor in prolonging the manifestations of the disease. Thick bands or more delicate "cobweb" adhesions bind the tubes and ovaries to adjacent surfaces and often form a tough matted mass which may implicate the appendix, the pelvic colon and the dependent coils of the ileum. The disease is usually bilateral though often more severe on one side than the other.

### PNEUMOCOCCAL PERITONITIS

This form of peritonitis occurs principally in children. Two varieties are recognized according as the disease appears to arise primarily or is secondary to pneumococcal affection elsewhere.

**Primary Pneumococcal Peritonitis.** This is almost restricted to female children. The disease occurs with greatest frequency between the ages of three and seven years. It has been suggested that infection reaches the peritoneum from the genital tract. Pneumococcal peritonitis is rare in well cared for children, but is apt to attack those living in squalid surroundings in whom the vulva and vagina may be contaminated with infective material. In smears taken from the vagina of neglected children pneumococci may be demonstrated, and in many cases of pneumococcal peritonitis the organism may be cultivated from the vaginal secretion which, in a few cases is purulent. The fact that the organism from the vagina is of the same type as that in the peritoneum has suggested that the infection is an ascending one. After the age of seven or eight years the vaginal secretion becomes acid and presumably inhibits infection.

More recent work, however, suggests that pneumococcal peritonitis is usually the result of infection by blood borne organisms. In some cases the peritoneal infection is merely part of a pneumococcal septicæmia, in other cases the peritonitis assumes the rôle of a

fixation abscess and may therefore be regarded as a beneficent reaction.

In the early stages of pneumococcal peritonitis there is an oily or sticky exudate in the pelvis, and the peritoneum is very congested. Later the exudate becomes watery or slightly blood stained, and eventually purulent, and there may be flakes of fibrinous lymph, which adhere to the peritoneum or to the intestine. The fimbriae of the uterine tubes show a fiery hyperaemia, and pus, containing pneumococci, can be expressed from their lumen. The interior of the tubes presents the signs of catarrhal inflammation. In some, especially in older children, the process is more chronic, and the infection becomes localized by adhesion of the intestines and the omentum, so that a large pelvic abscess results. The process may be sufficiently chronic to create confusion with tuberculous peritonitis or sufficiently acute to simulate acute appendicitis. The abscess may rupture at the umbilicus or into the bladder or rectum.

As primary pneumococcal peritonitis begins in the pelvis irritation of the pelvic viscera, especially the colon and bladder is the outstanding sign of the disease, and therefore the child suffers from frequent or painful micturition as well as from tenesmus and diarrhoea with much mucus or even blood in the stools. After peritonitis has persisted for a time the systemic effects of the pneumococcal infection become manifest and the pulse rate and respiration become rapid and toxæmia is severe. There is usually a considerable leucocytosis and in blood cultures the pneumococcus can often be found. In the later stages the systemic illness may completely overshadow the peritonitis. In young children the disease runs a rapid course and generally ends fatally, but in older children recovery may occur.

**Secondary Pneumococcal Peritonitis.** This occurs as a complication of some other pneumococcal lesion, such as pneumonia or empyema or, occasionally, otitis media. Either sex may be affected and though the disease is commoner in children it may occur in adults. Infection reaches the peritoneum by the blood stream and at the same time there may be other secondary pneumococcal manifestations such as pericarditis and meningitis. Any part of the peritoneal cavity may be involved. Sometimes the peritonitis is very localized in others it is widely diffused. The exudate may be serous or purulent. If recovery occurs a localized abscess may form.

Similar to secondary pneumococcal peritonitis is the streptococcal peritonitis that is sometimes seen in childhood. The organism is usually of a hæmolytic variety, and its source may be the nasopharynx or the lower respiratory tract. A few cases have been traced to the genital tract in females. The sexes are affected about equally.

### **STREPTOCOCCAL PERITONITIS**

The streptococci in peritonitis are frequently hæmolytic organisms of great virulence, and streptococcal peritonitis is consequently a grave infection. It may arise in the course of scarlet fever but is most common as a complication of puerperal endometritis. From the uterus the organisms gain access to the peritoneum along the uterine tubes, or

fixation abscess and may therefore be regarded as a beneficent reaction

In the early stages of pneumococcal peritonitis there is an oily or sticky exudate in the pelvis, and the peritoneum is very congested. Later the exudate becomes watery or slightly blood stained, and eventually purulent, and there may be flakes of fibrinous lymph, which adhere to the peritoneum or to the intestine. The fimbriae of the uterine tubes show a fiery hyperemia, and pus, containing pneumococci, can be expressed from their lumen. The interior of the tubes presents the signs of catarrhal inflammation. In some, especially in older children, the process is more chronic, and the infection becomes localized by adhesion of the intestines and the omentum, so that a large pelvic abscess results. The process may be sufficiently chronic to create confusion with tuberculous peritonitis or sufficiently acute to simulate acute appendicitis. The abscess may rupture at the umbilicus or into the bladder or rectum.

As primary pneumococcal peritonitis begins in the pelvis, irritation of the pelvic viscera, especially the colon and bladder, is the outstanding sign of the disease, and therefore the child suffers from frequent or painful micturition as well as from tenesmus and diarrhoea with much mucus or even blood in the stools. After peritonitis has persisted for a time the systemic effects of the pneumococcal infection become manifest, and the pulse rate and respiration become rapid and toxemia is severe. There is usually a considerable leucocytosis, and in blood cultures the pneumococcus can often be found. In the later stages the systemic illness may completely overshadow the peritonitis. In young children the disease runs a rapid course and generally ends fatally, but in older children recovery may occur.

**Secondary Pneumococcal Peritonitis** This occurs as a complication of some other pneumococcal lesion, such as pneumonia or empyema or, occasionally, otitis media. Either sex may be affected, and though the disease is commoner in children it may occur in adults. Infection reaches the peritoneum by the blood stream and at the same time there may be other secondary pneumococcal manifestations, such as pericarditis and meningitis. Any part of the peritoneal cavity may be involved. Sometimes the peritonitis is very localized, in others it is widely diffused. The exudate may be serous or purulent. If recovery occurs a localized abscess may form.

Similar to secondary pneumococcal peritonitis is the streptococcal peritonitis that is sometimes seen in childhood. The organism is usually of a hæmolytic variety, and its source may be the nasopharynx or the lower respiratory tract. A few cases have been traced to the genital tract in females. The sexes are affected about equally.

### STREPTOCOCCAL PERITONITIS

The streptococci in peritonitis are frequently hæmolytic organisms of great virulence, and streptococcal peritonitis is consequently a grave infection. It may arise in the course of scarlet fever, but is most common as a complication of puerperal endometritis. From the uterus the organisms gain access to the peritoneum along the uterine tubes, or

directly through the uterine wall, or by way of infected thrombi in the large uterine veins. The disease may remain localized to the pelvis, but often spreads diffusely over the greater part of the abdomen. The fluid exudate is thin, watery and often sanguineous, and it contains few pus cells but immense numbers of organisms. A striking feature is the great dilatation of the gut, and the laxity of the abdominal wall after childbirth allows the distension to proceed to an extreme degree, so that the abdominal enlargement even exceeds that of pregnancy.

*Post-operative peritonitis* also is often due to streptococci, though coliform bacilli predominate. The condition may arise from soiling of the peritoneum at operation or from some subsequent cause, for example, from leakage at an anastomosis, but in some cases the source is not discoverable. In such circumstances a hæmatogenous infection from distant septic foci may be incriminated, but there is good reason to suppose that most frequently there has been contamination at the time of operation, from faulty technique.

Post-operative peritonitis is remarkable in that many of the usual signs of peritonitis are absent. There may be no pain, no abdominal rigidity and no rise of temperature, but only gradually increasing distension and duodenal decline.

### TUBERCULOUS PERITONITIS

Tuberculous peritonitis may affect persons of either sex and at any age, but it is commonest in childhood and early adult life. In the majority of cases infection is derived by direct extension from some primary focus within the abdomen, such as a tuberculous ulcer of the small intestine, mesenteric lymph glands, or a tuberculous uterine tube. Sometimes infection is blood-borne from foci elsewhere or there may be active tuberculosis in the lung and pleura or elsewhere.

*Acute Tuberculous Peritonitis.* Acute tuberculous peritonitis may occur alone or as part of a generalized miliary infection. The peritoneum becomes covered by numerous minute greyish tubercles and a fluid exudate usually of a serous character accumulates. Since the spleen is enlarged and a lymphocytosis is present the condition is liable to be mistaken for typhoid fever, especially as the constitutional disturbances are very similar.

A suppurative type of tuberculous peritonitis occurs, but is distinctly rare. It is seen chiefly in young girls and is usually secondary to disease of the uterine tubes. The peritoneum becomes thickened and cedematous, and covered with jelly-like exudate. Tubercles are scattered over the surfaces, but are often obscured by the thick exudate. The effusion, which may fill the whole abdominal cavity or be restricted to one part of it, is thick, grumous and often of a greenish colour. The disease runs a rapid course, with pronounced emaciation and a hectic temperature. If untreated the abscess may come to the surface, usually at the umbilicus, and a fecal fistula may result.

*Chronic Tuberculous Peritonitis.* This is considerably more common than the acute form, and is usually due to spread of infection from the small intestine, from a caseous mesenteric lymph gland, or from the

uterine tube Three distinct clinical types may be recognized (1) the ascitic type, (2) the dry or adhesive type, and (3) the encysted type

(1) The ascitic type usually affects children or young adults, but occasionally occurs in later life The tubercle bacilli, disseminated through the peritoneal cavity from a primary focus, are implanted on the peritoneal surfaces, and innumerable yellowish grey tubercles develop, varying in size from that of millet seeds to peas or even larger They may be confluent and give rise to a considerable mass

A fluid exudate gathers in the peritoneal cavity, and may eventually collect in such large amount that the abdomen becomes distended, the skin stretched and shiny, and the superficial veins dilated Such a prominent abdomen contrasts strangely with the emaciated thorax and extremities In boys a patent processus vaginalis may become filled with the fluid, and its peritoneal lining the seat of tubercles The fluid is serous in character, usually clear and straw coloured but sometimes turbid or even blood stained Microscopically it is found to contain lymphocytes in excess Bacilli can rarely be demonstrated, even after centrifugalization, but their presence can be proved by guinea pig inoculation

(2) The dry type is characterized by formation of extensive adhesions, which bind together adjacent viscera especially coils of ileum This form is usually limited to one part of the abdomen and is especially marked around the primary focus of infection, for example a caseous mesenteric gland Intestine coils adhere and these together with the thickened mesentery and omentum may sometimes be felt as an irregular doughy swelling Caseation within the mass is common Sometimes the omentum is infiltrated with tubercles and becomes bunched up into a firm cylindrical mass, which may be felt lying across the upper abdomen Often the parietal peritoneum is greatly thickened and oedematous and in some cases so extensive are the adhesions or the viscera to the abdominal wall that exploration is impossible Fistulae are common in this form of disease, either between various portions of the intestinal tract or to the exterior Another complication of some frequency is intestinal obstruction which, however, seldom culminates acutely Even if the condition resolves there will still remain a grave risk of obstruction or even strangulation from adhesions

(3) The encysted form is rare It may be regarded as a combination of the other two types, for there is a localized collection of fluid in a region bounded by fibrous adhesions The fluid collection is often situated in the pelvis, and in women it is liable to be mistaken for an ovarian cyst Since the fluid is walled off by adhesions of intestinal coils the swelling may be tympanitic on percussion Apart from the localized collection the remainder of the peritoneal cavity may be free from disease

### BILIARY PERITONITIS

Intraperitoneal extravasation of bile may follow injury to the biliary tract, it may result from perforation of the gall bladder in acute cholecystitis, or it may occur without demonstrable cause Its effects depend principally upon the presence or absence of infection,

for in man, unlike certain laboratory animals, a sterile effusion of bile leads to remarkably little disturbance, probably because human bile contains comparatively little of the toxic bile salt, sodium tauracholate

(1) Biliary extravasation due to trauma is generally a sequel to a severe crush injury rupturing the bile ducts close to the porta hepatis. Bile accumulates in the peritoneal cavity, sometimes painlessly, and reabsorption of its pigment leads to jaundice. In some cases a remarkably large amount of bile escapes. In the case reported by Barlow in 1844 32 quarts of pure bile were evacuated by paracentesis during three months with ultimate survival.

(2) Biliary extravasation due to cholecystitis occurs mainly in fulminating infections in elderly persons. The perforation may be a large one or so small as to be barely visible, as in Leriche's case, in which the bile filtered through an apparently intact gall bladder wall, 'a veritable biliary dew'. The fluid is highly infective and leads to diffuse peritonitis which in nearly 50% of cases proves fatal.

(3) Biliary extravasation without obvious cause, the so called "perforationless biliary peritonitis," has only recently been recognized. The extravasation occurs suddenly, with symptoms suggesting a gastric or duodenal perforation. There is free bile in the peritoneal cavity, and the extraperitoneal tissues round the common bile duct are discoloured or almost necrotic, but there is no evident perforation and neither the site nor the cause of the leakage is apparent. It seems likely that in most cases there has been a minute perforation of the common duct which has healed spontaneously. The perforation has been attributed to rupture of a glandular crypt in the duct wall, to ulcerative cholangitis, or even to erosion of the mucosa of the duct by reflux of pancreatic juice from the biliary ampulla.

### SUBPHRENIC ABSCESS

Subphrenic abscess is a sequel of infection elsewhere in the abdomen. The toxæmia to which it gives rise and the inaccessibility of the infective process account for the anxiety with which it is regarded.

In the majority of cases subphrenic abscess follows an intra-abdominal suppurative lesion, and of these fully 50% are attributable to gastric or duodenal affections and to appendicitis, the remainder to diseases of the liver and bile passages, or of the intestines, kidneys or pelvic organs. Occasionally a subphrenic abscess follows infection above the diaphragm such as empyema, but it is remarkable that transdiaphragmatic spread is much less common from thorax to abdomen than in the reverse direction. Rarely a subphrenic abscess follows hæmatogenous infection from a distant source.

Anatomically, the subphrenic region is divided into six potential spaces by the cruciform arrangement of the peritoneal ligaments of the liver, and Barnard has emphasized that infections are often limited to one of them, and that the particular space infected depends upon the site of the original disease and the avenue of infection. Of the six

potential spaces there are three on each side of the mesial plane, two intra and one extra peritoneal

The right anterior intraperitoneal space is the upward prolongation of the main peritoneal cavity in front of the liver, and it occupies a position under the right vault of the diaphragm. The right posterior intraperitoneal space is subhepatic rather than subphrenic, and is usually described as the subhepatic or right kidney pouch. The right extraperitoneal space corresponds to the "bare area" of the liver, between the layers of the coronary ligament.

On the left side the anterior intraperitoneal space occupies the left vault of the diaphragm in front of and above the stomach, the posterior intraperitoneal space is merely the upper part of the omental bursa, and the extraperitoneal space does not exist in health, but appears where pus, collecting around the upper extremity of the left kidney, separates the peritonium from the diaphragm.

The avenue by which infection reaches one of these spaces varies in different cases. From a perforated duodenal ulcer infected fluid is diverted to the right of the mesial plane by the projection formed by the vertebral column, and under the influence of gravity and the aspiration action of the diaphragm, the fluid usually reaches the subhepatic or right kidney pouch (right posterior intraperitoneal space). A gastric ulcer on the anterior aspect of the smaller curvature readily infects the left anterior compartment, and one on the posterior aspect leaks directly into the omental bursa (left posterior intraperitoneal space). Appendicitis usually leads to abscess formation in one of the compartments on the right side, the intraperitoneal spaces are liable to be involved as a result of a fairly diffuse peritonitis, and the extra peritoneal space may be infected by cellulitis spreading along the retro-cæcal connective tissues.

It is important to recognize that a subphrenic abscess is not always a single large cavity, and that there may be several pockets communicating by narrow channels or separated by soft adhesions. The pus is thick, and often contains necrotic areolar tissue. Gas may be present, either from the action of gas producing organisms or as a result of leakage from a hollow viscus such as the stomach. When the abscess is situated towards the front it may displace the liver downwards and approach the skin surface below the costal margin, but often the liver is extensively fixed by adhesions, and the abscess then elevates the diaphragm. Elevation and fixation of the diaphragm indeed constitute a significant radiological evidence of subphrenic abscess.

The infecting organism is most commonly *B. coli*, often mixed with streptococci. Not infrequently anaerobes are present.

A subphrenic abscess may undergo resolution or become chronic, but much more often it progresses, and if unrelieved proves fatal. In rare cases it may rupture spontaneously into the lung, pericardium or stomach or even at the skin surface. Frequently the condition is complicated by basal pleurisy and reactionary effusion. Adhesions bind the elevated diaphragm to the parietes and obliterate the costophrenic sinus, an effusion collects in the pleural cavity, clear or purulent, but in either case often sterile.

## TUMOURS OF THE PERITONEUM

Primary tumours of the peritoneum are extremely rare, and indeed it is doubtful if they exist. Many supposed peritoneal tumours have been described but in most cases there has been no conclusive proof of their peritoneal origin, and it is suspected that many alleged examples are either secondary growths or tumours arising from the extra peritoneal tissues.

Secondary tumours on the other hand, are common. In the great majority they are metastatic deposits from primary growths within the abdomen most often in the stomach, ovaries or large intestine. In other cases they are derived from more distant sources, for example, the breast.

Dissemination of free tumour cells through the cavity of the peritoneum may take place at any time after the growth has reached the serous surface. Once set free tumour cells may be implanted in any part of the cavity and there proliferate. Generally the cells gravitate towards the pelvis and form multiple nodules over the pelvic floor, and sometimes one may even grow to such a size as to be palpable *per rectum*. Such a mass in the pelvis may simulate a primary tumour growing from the colon or pelvic organs, especially if the actual primary lesion is relatively symptomless. Often the malignant cells become implanted on the surface of one or both ovaries, and there set up secondary growths, which may attain considerable size. The so called Krukenberg tumour arises in this fashion. It is a secondary carcinoma derived from a primary growth in the stomach, colon or other organ, and its special feature is the presence of globules of clear mucoid material within the cells with displacement of the nucleus creating a 'signet ring' appearance. The delayed appearance of gastric or intestinal symptoms renders such tumours very liable to be mistaken for primary growths of the ovary.

In other cases tumour cells floating freely in the peritoneal cavity are caught in the great omentum and proliferate to form a bulky sausage shaped or apron like mass readily palpable through the abdominal wall.

One of the most outstanding features of secondary peritoneal involvement is a fluid exudate. A small amount of free fluid may be present before any definite nodules are visible or palpable and when found at exploratory operation is very suggestive. In the later stages the exudate increases and causes great abdominal distension. The fluid at first may be clear, but is usually blood stained and on microscopic examination tumour cells may sometimes be found.

*Tumours of the great omentum* are almost always secondary to growths in other parts of the abdomen, most often in the stomach, colon, ovary or gall bladder. Primary sarcoma of the great omentum has been described but is extremely rare.

## PSEUDOMYXOMA PERITONEI

This remarkable condition is characterized by masses of gelatinous or mucoid material in the peritoneal cavity, either localized to a particular region or more widely diffused. It occurs as a complication of two



entirely different pathological lesions, which superficially appear to possess little in common, namely, cystic tumours of the ovary and mucocele of the appendix

(1) **Secondary to Ovarian Tumours** In most cases the primary lesion is a pseudomucinous cystadenoma, and the peritoneal involvement is usually attributed to the rupture of one of the cysts, with escape of its contents. Pseudomyxoma peritonei may, however, be present where there is no evidence that a cyst has ruptured, and perhaps more surprising still, it practically never follows accidental rupture of a cyst during operation

The peritoneal cavity becomes filled with immense quantities of yellowish jelly like material, which may be scooped out in handfuls. In some cases it is distributed diffusely in homogeneous layers and insinuates itself into all recesses of the cavity, even to the subphrenic space, in others it is circumscribed into large globular masses which lie between intestinal coils or in the pelvis

It is now acknowledged that the jelly is not colloid or even mucoid but is almost always composed of pseudomucin though occasionally true mucin is present. Its mode of formation is not understood. It has been regarded as a product of the lining cells of the peritoneal cavity, a response to the irritation of the fluid exuded from the primary tumour, but it is difficult to accept this explanation because no comparable reaction on the part of the peritoneum has been witnessed in other diseases. The generally acceptable view is that the pseudomucin is elaborated by the cells of the primary tumour, although such cells are usually scanty and difficult to demonstrate

Whatever its origin, the exudate causes a form of low grade inflammatory change in the peritoneum. Fibrin forms and surrounds the jelly material with a delicate capsule, which later is fibrotic. Fine strands of fibrous tissue also traverse the jelly and fix it to the peritoneum so that at operation the masses are separated with some difficulty, leaving behind stringy, viscid tags. The general peritoneal membrane may also show reactionary changes

(2) **Secondary to Disease of the Appendix** A number of cases have been described in which a form of pseudomyxoma peritonei has followed appendiceal disease. In some, a mucoid carcinoma of the appendix has probably been responsible. In others, there has been a mucocele of the appendix or a diverticulum, which has ruptured, disseminating its contents. It is not known whether the gelatinous material is the result of peritoneal irritation, or whether it is the product of mucus secreting epithelial cells that have been set free from the appendix. There is a further possibility, namely, that the ruptured mucocele remains in free communication with the peritoneal cavity, and thus continuously discharges its secretion

The effects are very similar to those described in relation to ovarian cysts, but they are more frequently localized to the immediate neighbourhood of the appendix, and only rarely become widespread. The appendix is buried in a gelatinous mass the size of a small orange, or even larger and the neighbouring peritoneal surfaces show reactionary changes with fibrosis

## TORSION OF THE OMENTUM

Abnormal fixation of the great omentum, as within a hernial sac or from adhesion to a viscus, may provide an obvious axis for rotation. There are cases, however, in which torsion may affect a seemingly healthy omentum. It has occurred most often in adults over thirty years who have recently become obese, but the underlying cause (as applies to torsion of organs in general) remains obscure, although venous engorgement followed by elastic recoil of arteries is a current explanation of its origin. The twist is always clockwise and may be a single rotation or as many as eight. The obvious effect is strangulation, and it is therefore not surprising that the omentum forms a palpable swelling and that a blood stained effusion develops within the abdomen. The condition is important in that it may simulate appendicitis or cholecystitis.

## TUBERCULOSIS OF THE MESENTERIC LYMPH GLANDS

The lymph glands in the abdomen especially those draining the lower part of the ileum and the first part of the colon, are commonly the seat of tuberculous infection. Indeed, in Scotland it is still common primary sites of tuberculosis, especially in childhood. General experience suggests that this is not true in other parts of the world. Tuberculosis of the lymph glands in its active form occurs in children or young adults and may be responsible for prolonged ill health and intestinal disturbances. Later calcification is evidence that at an earlier date the glands have been the site of caseation.

The glands are infected by way of the intestine, and probably milk is the common vehicle by which the tubercle bacillus is conveyed to the body but in most cases of tuberculous adenitis the intestinal lesion is not obvious. Sometimes only one gland is diseased, but more often several are involved. At first the glands are discrete and firm, and only a few points of caseation are found in each. Later groups of glands are affected, and an irregular confluent mass results which may be palpable. Such a mass is situated most often in the ileocecal region, but similar masses may be present at higher levels in the mesentery. Sometimes the tuberculous lymph glands soften and form abscesses. Rarely such an abscess ruptures into the peritoneal cavity and may give rise to generalized (though not necessarily fatal) peritonitis.

Tuberculous mesenteric glands tend to heal by fibrosis and if they are caseous, calcification is the usual result. Localized fibrosis of the mesentery may result in contraction with angulation of the intestine. Adhesion of a loop of intestine to the surface of a tuberculous gland is of fairly frequent occurrence, and may cause kinking by obstruction. In a few instances a mass of tuberculous glands situated at the root of the mesentery of the small intestine has by pressure led to duodenal ileus. Cases have been observed in which the prolonged irritation from calcified glands in the pelvic mesocolon has resulted in megacolon.

In radiographic investigation of lesions outside the intestine, the shadows of calcified tuberculous lymph glands may create confusion

When the shadows are in the region of the kidney or in the line of the ureter they may simulate calculi in these organs. The shadows of calcified glands are often multiple but in density are not so uniform as those of calculi, and they may alter their position on change of posture.

### EMBOLISM AND THROMBOSIS IN THE MESENTERIC BLOOD VESSELS

Occlusion of the mesenteric vessels may involve the arteries or the veins, and in either case it usually leads to infarction of a part of the intestine. Venous occlusion is always due to thrombosis, but arterial occlusion may result from primary thrombosis or from the impaction of an embolus. Rupture of the mesenteric vessels, as may occur from a crush or blast, if not fatal from hemorrhage, may produce the same effects.

In surgical practice these lesions are rare. They occur usually in subjects past middle life with disease of the circulatory system, and they give rise to a very acute and generally fatal illness. Diagnosis can rarely be made with certainty before the abdomen is opened.

The anatomical peculiarities of the mesenteric circulation require consideration in order that the mechanism of infarction may be understood. The anastomosis between the superior and inferior mesenteric arteries through the ascending branch of the inferior mesenteric and the middle colic artery is a slender one, and if the superior mesenteric artery be suddenly obstructed the inferior mesenteric is insufficient to compensate for its loss, although when occlusion is gradual a collateral circulation may be established. Collateral circulation in the mesentery of the small intestine is very free through the channel of arterial arcades that connect the twelve or more mesenteric vessels, but not through the arteries that pass from the terminal row of arcades to the gut. These arteries are known as the vasa recta. They are short vessels and do not communicate freely with one another in the mesentery or on the surface of the bowel. Consequently if the vasa recta or the distal arcades are obstructed the vitality of the affected portion of intestine is imperilled. The disposition of the mesenteric veins, though not so uniform, corresponds roughly to that of the arteries.

#### Arterial Occlusion

Embolism accounts for the majority of cases of arterial occlusion. The inferior mesenteric artery, on account of its small diameter, is rarely entered by an embolus but the superior artery is of larger calibre and, at its origin, runs almost parallel to the aorta, and is consequently more often occluded. An embolus may originate in the heart or in the aorta or sometimes from a pyæmic infarct in the lung that has led to septic thrombosis of the pulmonary veins. An embolus from the heart usually takes the form of an organized vegetation from the mitral or, less often from the aortic valve, and it may be detached during the acute stages of endocarditis or at a remoter period. Emboli

from the aorta usually arise from organized clot formed on an atheromatous plaque or ulcer

The superior mesenteric trunk and its larger branches are affected with about equal frequency. The effect of the impaction of the embolus in the main trunk is to cause immediate arrest of the circulation distally. Venous flow in the mesentery ceases, and, as there are no valves in the portal veins venous engorgement occurs from backflow in the mesenteric veins. Finally, infarction of the intestine occurs. If the embolus is arrested lower down in the mesenteric artery or in one of its larger branches the collateral vessels are sufficient to maintain the circulation, and would suffice to keep the intestine alive were it not for a secondary thrombosis that usually extends centrifugally from the site of the embolus. If thrombosis reaches the terminal arcades or the vasa recta infarction is inevitable.

Primary thrombosis in the mesenteric arteries is very rare. It may occur as a result of extension of atheroma of the abdominal aorta, from thrombosis arising in an aneurysm of the superior mesenteric artery and rarely in association with thromboangitis obliterans. Continental writers have suggested that local arteriosclerosis of the mesenteric arteries may cause thrombosis, and that such narrowing may be a cause of painful intestinal crises in elderly subjects.

### Venous Occlusion

Thrombosis in the mesenteric veins may be secondary to obstruction in the portal vein, *e.g.*, from pressure of tumours or in cirrhosis, but it is more often initiated by infective processes in the viscera drained by them.

Appendicitis with suppuration is responsible for most cases. The thrombosis is of an infective character and usually leads to portal pyæmia with abscesses in the liver (*see* p 574). The pylephlebitis, which is commonest in the ileocolic vein, may be found at operation, but more often it arises as a post-operative complication. Its frequency is less than 1 per 1 000 cases of acute appendicitis.

Simple thrombosis of the veins may, in rare instances, be compensated through collateral vessels but if the process extends to or originates in the peripheral arcades or their tributaries, infarction ensues.

### Results of Mesenteric Vascular Occlusion.

The pathological effects of mesenteric vascular occlusion, general and local, are similar to those of strangulation of the intestine and are dependent on the length of bowel involved (*see* p 496). Hæmorrhagic infarction is the usual result. Whether the obstruction is arterial or venous the intestine and mesentery become congested, swollen and oedematous. Blood stained serous fluid is exuded into the peritoneal cavity, and a hæmorrhagic exudate forms in the lumen of the bowel. With the onset of infarction the intestine assumes a dull purple shade, loses its elasticity, and finally becomes gangrenous. The whole small intestine or a small section of it may be involved. The

line of demarcation is rarely abrupt. At operation the mesentery is very turgid and friable, and is pulseless over a wide area.

Mesenteric occlusion results in a fulminating abdominal illness with features simulating intestinal obstruction or internal hæmorrhage. The swollen intestine may give rise to a palpable tumour and, if mælena is present, the resemblance to intussusception may be very close.

Operative treatment aims at resecting the devascularized area of intestine and mesentery in the hope of arresting the spreading thrombosis and averting toxic absorption. Success has followed removal of as much as 14 feet of the small intestine.

## RETROPERITONEAL AND MESENTERIC CYSTS AND TUMOURS

The majority of cysts and tumours in the retroperitoneal tissues or mesentery arise from the pancreas, kidneys, adrenals, and lymph glands, and are described in their respective chapters. There remain, however, a certain number which arise otherwise, and it is to them that the terms retroperitoneal or mesenteric cysts and tumours are usually applied.

The classification of these conditions is unsatisfactory, for some are simple retention cysts, others are cystic tumours, and yet others are solid tumours. They may arise either between the layers of the mesentery or mesocolon or in the retroperitoneal areolar tissues. Cysts in the mesentery tend, as they enlarge, to expand the base of the mesentery and eventually to assume a retroperitoneal position, and cysts arising in the retroperitoneal tissue sometimes bulge between the layers of the mesentery.

In general these retroperitoneal or mesenteric swellings tend to displace the viscera forwards and they may cause symptoms by pressure on the stomach or intestines. The ureter, being adherent to the posterior parietal peritoneum, may be compressed, and secondary hydronephrosis occur.

### Cysts

The following classification of retroperitoneal cysts has been suggested —

- (1) Traumatic blood cysts arising from an encapsuled hæmatoma
- (2) Inflammatory tuberculous cysts arising from glandular infection
- (3) Parasitic hydatid cysts, usually secondary to echinococcus disease of the liver
- (4) Neoplastic cysts arising from the degeneration of tumours
- (5) Dermoid cysts
- (6) Developmental cysts

Only the last variety requires further consideration.

Developmental cysts are generally unilocular cysts of simple structure. They lie in the retroperitoneal fatty tissues and are unattached to their surroundings except by areolar tissue. The wall of the cyst is composed of fibrous tissue and may be thin and almost translucent or very

thick. Sometimes there is a lining membrane of columnar, cuboidal or flattened cells. The content is usually a straw-coloured watery fluid of low specific gravity, or it may be blood stained or chylous. Rarely a multilocular cyst may contain chylous and clear fluids in separate compartments.

The origin of these developmental cysts is not clearly determined and it seems possible that it varies in different examples. The following possible modes of origin have been suggested: (1) lymphatic; (2) enterogenous, (3) mesocolic, (4) urogenital.

*Lymphatic cysts*, arising from dilatation of lymph vascular networks present in embryonic life are known to occur in the neck, where they form large thin walled cavities present at birth (cystic hygroma), and it is possible that some retroperitoneal cysts have a similar origin.

*Enterogenous cysts* are very rare, and almost always they are situated close to the ileocecal region. They are believed to originate in congenital diverticula of the small intestine which have lost their continuity with the gut.

*Mesocolic cysts* are believed to originate from failure of coalescence of the two posterior layers of parietal peritoneum during the third stage of intestinal rotation (*see p. 488*). It is said that the persistence of small islands of peritoneum in such circumstances is responsible for some retroperitoneal cysts containing watery fluid.

*Urogenital cysts* are probably the commonest form of developmental retroperitoneal cysts. They are derived from rudiments of the mesonephros (Wolffian body) or from other sequestered portions of the developing genito-urinary system. Generally they are simple unilocular cavities containing clear watery fluid, but they may be multilocular, and occasionally they resemble the multilocular cystic tumours of the ovary.

### Tumours and Cystic Tumours

*Sarcoma* is the commonest retroperitoneal tumour. It occurs most often in the perinephric region, and principally affects young persons. Round-cell and spindle-cell varieties are described. In its growth and pathological characters it resembles sarcoma in other parts of the body.

*Neuroblastoma* (sympathicoblastoma) is not uncommon in young children, in whom it forms a rapidly growing tumour of great malignancy. It arises from the autonomic system, and closely resembles tumours of the adrenal medulla (*see p. 604*).

*Ganglioneuroma* may arise in the retroperitoneal tissues, or occasionally in the mesentery. It too arises from the autonomic chain, and resembles tumours of similar origin arising from the adrenal medulla and in the mediastinum. Typically, it is a firm rounded tumour which grows slowly to considerable size and remains encapsuled, but occasionally assumes malignant characters. Microscopically, it contains medullated and non medullated nerve fibres and numerous ganglion nerve cells.

*Lipoma* in the retroperitoneal tissues is not uncommon. A liposarcoma or mixed fatty tumour has been described, which is characterized by a tendency to infiltrate widely in the retroperitoneal space and

even into the vertebral canal. To the naked eye it somewhat resembles a lipoma, but microscopically areas of sarcomatous infiltration are evident.

*Teratoma* in the retroperitoneal tissues may be solid or cystic and may attain large size and cause pressure symptoms. The tumour is believed to arise from misplaced totipotent cells from the blastomere, or from aberrant sex cells. It occurs principally in women.

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## CHAPTER XXVIII

# DISEASES OF THE GALL-BLADDER, LIVER AND BILE DUCTS

## FUNCTIONS OF THE GALL-BLADDER

DESPITE the common observation that cholecystectomy causes little or no digestive disturbance there can be no doubt that the gall bladder is by no means functionless, and experimental researches suggest that it plays a valuable part in the physiology of the biliary system

(1) **Concentration of Bile** As early as the eighteenth century it was recognized that during its stay in the gall bladder the bile becomes darker and of less watery consistence, as though concentrated, and in recent years clear proof of such a process has been forthcoming from the experimental work of Rous and McMaster. These workers, making use of the fact that in the dog one of the hepatic ducts enters the common bile duct below the level of the gall bladder, were able to separate by ligature two systems of bile ducts—one connected with the gall bladder and one draining directly from the liver. By comparing the pigment content of bile derived from each of these systems, the degree of concentration of the bile which had entered the gall bladder could be estimated. From these experiments it becomes evident that the gall bladder is able to absorb water from the bile with great rapidity, concentrating the bile within the space of a few hours to a tenth part of its former bulk.

(2) **The Reservoir Function** The importance of the concentrating property lies especially in the fact that it enables the gall bladder, in spite of its small size, to act as an adequate reservoir for the bile, storing it in the intervals of digestion and pouring it forth into the duodenum as required. Secretion of bile from the liver is continuous, and from 20 to 30 ozs. are secreted in the course of 24 hours, but by concentration the volume is greatly reduced, and the gall bladder, whose capacity is about 2 ozs., is thus of adequate size.

(3) **Regulation of Pressure in the Biliary System** Whenever the sphincter at the lower end of the common duct is contracted the bile is dammed back in the duct system, but by concentration in the gall bladder and by the elastic expansion of this viscus the potential "back pressure" is countered, and the smaller intrahepatic passages are protected from distension. Evidence of the importance of this function is seen when a functioning gall bladder is removed, for some temporary dilatation of the whole duct system often then occurs. It is seen again, and in more obvious form in the early stages of complete obstruction of the common duct, for in this event a functioning gall bladder, by concentrating the bile and by becoming dilated, delays the increase of intraductal pressure and thus hinders the onset of obstructive jaundice.



(4) Relation to Cholesterol Much has been written on this subject, and directly opposite opinions have been expressed, some authorities believing that cholesterol is absorbed from the bile in the gall bladder, others that cholesterol is excreted by the vesical mucosa. At present absolute proof is lacking, but there is some evidence in favour of the former view. This will be considered again in relation to cholesterosis of the gall bladder.

(5) Discharge of Bile into the Duodenum The discharge of bile is governed by a reciprocal nervous mechanism between the sphincter of the common duct and the gall bladder, a mechanism whereby relaxation of the sphincter coincides with contraction of the gall bladder, and allows the expulsion of bile, whereas spasm of the sphincter leads to relaxation of the gall bladder and passive dilatation.

Contraction of the gall bladder with relaxation of the sphincter of the common duct occurs as a result of the presence of fats in the duodenum, and may follow the intraduodenal administration of various other substances, notably peptone and magnesium sulphate. Ivy and Oldberg have obtained similar results by the injection of an extract of intestinal mucosa resembling *secretin*, to which they give the name *cholecystokinin*. It is possible that a fatty meal may exert its effect on the gall bladder in a similar way by provoking the formation of some such hormone in the intestinal wall.

A reverse effect—relaxation of the gall bladder with spasm of the common duct sphincter—is produced by the administration of morphine. This drug, therefore, should be avoided when relaxation of the sphincter is desired, for example in cholangitis or after removal of the gall bladder.

## CHOLECYSTITIS AND GALL-STONES

There is a close relationship between cholecystitis and gall stones, for either may predispose to the other. Thus a gall stone developing as an aseptic formation may predispose to cholecystitis while on the other hand an infection of the gall bladder, primarily non-calculous, may lead to the formation of stones.

Four possible states or sequences may therefore be recognized: (1) aseptic gall stones in a healthy gall bladder, (2) gall stones, initially aseptic, complicated by cholecystitis, (3) non-calculous cholecystitis, (4) cholecystitis, initially non-calculous, complicated by the development of 'septic' stones. And finally, by the combination of the second and the fourth sequences (5) aseptic stones complicated by cholecystitis and by secondary "septic" stones.

## GALL-STONES

It is often stated that there are three principal circumstances that predispose to gall stone formation: (1) infection of the gall bladder, (2) stasis of bile, and (3) increase in the cholesterol content of the blood. This statement is to some extent true, but it must be qualified by

consideration of the different varieties of stone, for these are very different in appearance and in chemical constitution and it is consequently entirely irrational to postulate a common cause

Gall stones may be classified in three principal types (a) pure pigment stones (b) pure cholesterol stones and (c) stones of mixed constitution Following the work of Aschoff and Baumeister it seems most rational to regard stones of the first two types as aseptic formations resulting from derangement in the metabolism of pigment and cholesterol respectively and stones of the third type as resulting from inflammatory processes

(a) Pure pigment Stones (Calcium Bilirubinate) In most



FIG 251 Cholesterol gall stones (unripe mulberry type) in a gall bladder affected by cholesterosis

(Department of Surgery University of Edinburgh)

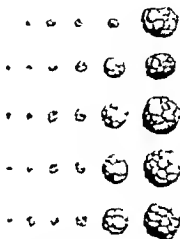


FIG 252 Gall-stones from a strawberry gall bladder The smallest stones are composed of bile pigment The larger ones consist of lobules of cholesterol deposited upon minute nuclei of pigment. All stages of the process are seen.

(Department of Surgery University of Edinburgh)

countries these stones are uncommon though they are said to be the most frequent type in Japan They are multiple, small and dark and are usually of metallic hardness and smooth. Occasionally they are large and irregular in shape Some of them arise in the smaller hepatic ducts as bile thrombi others appear to originate in the gall bladder They are particularly common in those circumstances in which there is excess of pigment in the bile as in haemolytic jaundice As a rule they cause little disturbance for they pass readily along the ducts to the duodenum but they may occasionally give rise to symptoms or may form nuclei for cholesterol deposition and thus lead to the formation of larger stones (see Fig 252)

(b) "Pure Cholesterol" Stones (95% to 98% cholesterol) are light

yellow in colour, or even pure white, and are rounded or oval, with a smooth or slightly nodular surface. They are usually single (the cholesterol "solitaire" of Meckel v Hemsbach), or there may be two or three, or even several. Such multiple stones have been compared to unripe yellow mulberries.

Stones of this type are often found associated with cholesterosis, or they may occur in a perfectly healthy gall bladder, and it appears certain that they arise from metabolic disorders rather than from infection. Cholesterol is normally present in large quantity in the bile, but is held in colloidal solution by the bile salts, and it is not surprising that cholesterol deposition may result either from an excess of cholesterol or from lack of solvent bile salts. Once the cholesterol is thrown out of solution it follows recognized physical laws and tends to aggregate in a single mass, which gradually increases in size over a long period. In a certain proportion of cases the cholesterol is deposited round preformed calculi of "pure pigment" type (see Fig 252).

The close relationship of pure cholesterol stones to cholesterosis of the gall bladder is a point of some interest. It has been suggested that the stones originate as "lipoid polypi" which have become loosened from the gall bladder wall and set free in the bile, but it seems more probable that both stones and cholesterosis result from a common causative factor, an increase in the cholesterol content of the bile.

(c) **Stone of Mixed Composition (Calcium, Cholesterol, Bilirubin)** These are the common gall stones. They are usually multiple, sometimes numbering several hundreds, and are then always faceted by mutual pressure. Less commonly a single large oval stone is present, perhaps forming an accurate cast of a shrunken gall bladder, or there may be three or four large barrel shaped stones. The gall bladder may contain clear bile, or a brownish yellow debris known as biliary sand or mud. The stones are usually laminated, with a soft friable brownish centre rich in cholesterol, which is surrounded by alternate bile stained and pale laminae rich in calcium.

These stones are generally believed to result from infection. In many cases culture yields a growth of organisms, but not uncommonly it is found that the stones and the bile or biliary mud are sterile,

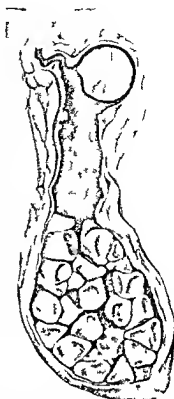


FIG 253 Gall bladder containing stones. A pure cholesterol stone of aseptic origin impacted in a saccular dilatation close to the cystic duct has redistributed to the formation of multiple faceted septic stones.

and even the gall bladder wall may yield no growth. In these cases it may be supposed that a previous infection has died out.

It is found that 'mixed' stones, even when very numerous are usually all of one size, or in two or three successive "hatchings" or crops and it may therefore be presumed that the predisposing factors concerned are not constantly present, but are apt to pass off and recur. According to Aschoff the essential predisposing factor is the occurrence of a mild acute or subacute cholecystitis with temporary occlusion of the cystic duct and temporary collection of mucus in the gall bladder. Stone formation occurs subsequently, when the inflammation has subsided and the cystic duct again becomes patent. When fresh bile enters and meets this purulent magma, mutual precipitation occurs, and soft concretions form which later become moulded to stones. Quite commonly in addition to one or more crops of faceted stones, there is a single rounded stone of larger size, often wedged in the sacular dilatation (Hartmann's pouch) close to the cystic duct (see Fig 2-3). This is a combination stone consisting of a central pure cholesterol stone encrusted with secondary mixed deposits. On Aschoff's theory it is to be regarded as a primary aseptic stone which later, by occluding the cystic duct, has given rise to the formation of multiple septic stones.

**Rarer Varieties of Stones.** Stones composed principally of calcium carbonate are uncommon. They are usually rounded and fairly hard, and are often white and chalk like in appearance. Occasionally *bilirubin* may replace the bilirubin of mixed or pure pigment varieties, giving a greenish colour to the stones. Rarely stones may form around foreign bodies portions of silk or catgut, or even round worms or liver flukes.

**Stones in the Bile Ducts.** Stones in the bile ducts are usually derived from the gall bladder whence they have passed into the common duct either along the cystic duct or by way of a fistulous communication. Occasionally, however, stones may arise primarily in the ducts, either as aseptic formations in the finer bile radicles (small pigment stones) or from the infection and biliary stasis associated with a stricture or obstruction of the common duct. Such stones in the ducts are said to be common in China owing possibly to the prevalence of liver flukes and other parasites.

Once a stone reaches the common duct its further progress depends upon its size compared to that of the sphincter at the lower end, for the common duct, since it has no muscular coat, is unable to expel the stone actively. The stone may be carried through a lax sphincter by the flow of bile and probably many small concretions are voided in this way. Larger stones may become impacted immediately above the sphincter and a stone in this situation may project under the mucosa into the duodenum and be most readily accessible at operation by the transduodenal route. More commonly the stone does not become fixed in position, but remains mobile within the duct, and by forming a kind of ball valve it gives rise to intermittent obstruction with jaundice. Occasionally, however a stone lies in the common duct for a long period, yet remains symptomless. At first the stone retains its earlier characteristics, and may be rounded, irregular or faceted. After a

short sojourn in the duct, however, it receives a coating of soft brownish *débris* and assumes an oval shape, conforming to the long axis of the duct. This putty like crust may break off when the stone is extracted at operation, and may form a nucleus for further deposits.

In a large proportion of cases the stone not only causes obstruction, partial or complete, but also renders the duct liable to infection. Indeed, cholangitis is rarely due to any cause other than stones. The common duct and all the smaller hepatic radicles become greatly dilated, and the bile becomes mixed with purulent *débris* and with "biliary mud." Cholangitic abscesses may develop and commonly lead to a fatal issue (*see p 575*).

**Recurrence of Stones after Operation** After cholecystostomy stones may recur from a simple recrudescence of the factors originally predisposing to stone formation—aided, no doubt, by the increased infection and scarring of the mucosa which are apt to follow drainage. In some cases a portion of catgut forms the nucleus for new stones. Not infrequently, a "recurrent" stone is one overlooked at a previous operation.

**Relation of Gall-stones to Pregnancy** It is a commonplace that gall stones occur characteristically in the "fair, fat and forty," and that the great majority of sufferers are parous women. In Naunyn's experience 90% of women with gall stones had borne children and not infrequently they may date the first onset of the symptoms of stones to the period of one of their pregnancies. It has been generally believed that child bearing predisposed to stone formation in virtue of the stagnation of the bile, the increased blood cholesterol content, and the greater susceptibility to infections during the later months of pregnancy.

It has been claimed by Gross, however, that the high incidence of gall stones in the parous is more apparent than real, and is simply due to the circumstance that more than four fifths of the adult female population is in the married state. Upon what appears to be adequate statistical evidence from the Leeds autopsy records, Gross found that in a large series of gall stone cases the proportion of married women to single approximated closely to that of the general population. Of 226 females with cholelithiasis, 89.8% were married, as compared with 86.6% of a large control series of females with no biliary disease. It would therefore appear that the influence of pregnancy upon gall stone formation is statistically insignificant. The special susceptibility of females to gall stones must be due to some factor other than the changes associated with child bearing.

**Gall-stones in Childhood** Gall stones are uncommon before the age of forty years, and are rare in childhood. There are, however, reported cases occurring in infancy and even in foetal life. Potter has recently collected 226 cases from the literature of gall bladder disease occurring before the age of fifteen years, including 140 cases in which stones were present. There were two examples in the foetus (sixth month and eighth month respectively), twelve in new born children and twenty eight in young infants. In some of the older children there was a history of typhoid fever or other infective disease of the abdomen, which may have been the ætiological factor. In others, the records

suggest that the stones were of pigment type, and were probably associated with excessive hæmolysis

**Gall-stone Ileus** Impaction of a gall stone in the intestine is responsible for approximately 1% to 2% of all cases of intestinal obstruction. The site of impaction in the majority of cases is the distal ileum, rarely the stone is arrested in the jejunum, at the ileo cæcal valve or in the colon

To obstruct the intestine a gall stone must necessarily be of considerable size 2 cm or more in diameter. Such a stone may reach the intestinal tract *via* the common bile duct (ulcerating through from the lower end of the duct into the duodenum) but this is a rare avenue, and in the majority of cases the stone gains access to the duodenum *via* a cholecyst duodenal fistula

Sometimes there is a long history of calculous cholecystitis culminating in an acute attack, and it is evident that the fistula has resulted from rupture of the acutely inflamed gall bladder into the adherent duodenum. More often there is no antecedent history and it is presumed that a large symptomless stone in the gall bladder has caused gradual pressure necrosis of the contiguous walls of the two viscera

After the stone has been extruded, the gall bladder becomes contracted, forming a small thick walled cavity, whilst the fistula may also become greatly reduced in size

The stone on reaching the duodenum may be carried to the ileum and impact within a few hours, or it may remain free in the intestine and acquire a shell of intestinal deposits

The obstruction which results is at first a partial one, and may remain so during several days, eventually it becomes complete as a result of spasm of the intestine and ulceration and infection of its mucous membrane

Lack of antecedent history, the variable character of the onset, and, in many, the absence of marked abdominal distension, render diagnosis difficult and are often responsible for dangerous delay in instituting treatment

### CHOLECYSTITIS

It has already been shown that cholecystitis may occur alone or as a sequel to gallstones. Generally, when cholecystitis occurs alone it is of mild type and since the clinical features also are slight, such cases do not often come to operation. The more severe forms are usually associated with the presence of gallstones

Unlike inflammation in most other situations cholecystitis generally begins insidiously and is of chronic type from the start. Acute cholecystitis occurs as a complication and as an incident in the course of chronic disease

### CHRONIC CHOLECYSTITIS

In health the gallbladder wall is translucent and transmits the blue green colour of the bile within. The earliest evidence of

cholecystitis is provided when this colour is lost and replaced by a dull yellow opacity. In more severe examples the wall is palpably thickened and of pearly white colour, and eventually the thickening may proceed to an extreme degree.

The mucous membrane at first is congested and oedematous, later it may become ulcerated, especially where pressed upon by stones, and eventually extensive scarring may develop, so that the inner surface is trabeculated with criss cross fibrous bands (see Fig 254). The scarring may lead to stenosis, either at the cystic duct or in the body of the viscus, and in the latter case may lead to some degree of hour glass deformity. Occasionally in very old standing disease the wall becomes extensively calcified so that it may be outlined in a radiogram (see also p 569).

The gall bladder may contain healthy bile but often the bile is pale and turbid and it may contain mucus, pus, stones, and the brownish yellow, cholesterol rich *débris* known as biliary mud. The stones may be loose, or they may fill the whole lumen and be closely packed in a solid mass. Occasionally they lie in small diverticula in the wall—parietal calculi.

Microscopically, the mucosa at first is often proliferated and projects in large bulbous or reduplicated folds which contrast strikingly with the delicate villi of the normal organ. Later other signs of chronic inflammation appear, there is an infiltration with small round cells the muscle coat is atrophied and fibroblastic and fibrous tissue pervades the whole wall.

Proliferation of the mucosa may lead to the formation of deep clefts lined by epithelium, which penetrate down to or even through, the muscularis and when cut obliquely in sections such formations may lead to an appearance like that of invading carcinomatous acini (Rokitansky Aschoff sinuses). These are to be distinguished from the somewhat similar crypts described by Luschka which are believed to be aberrant bile ducts traversing the gall bladder wall.

Occasionally the epithelial proliferation is more extensive, and leads to diffuse or localized thickening of the gall bladder wall which is honeycombed by epithelium lined crypts and glands, some of which may become cystic (cholecystitis glandularis proliferans).

## ACUTE CHOLECYSTITIS

Acute cholecystitis may occur as a primary event but much more commonly it arises as an incident in the course of chronic infection. The acute phase is usually precipitated by obstruction to the cystic duct as a result of impaction of a stone in this situation. It may thus properly be called "acute obstructive cholecystitis".

A stone may be impacted within the cystic duct proper or in the adjacent sacculation at the neck of the gall bladder (Hartmann's Pouch). If the content of the gallbladder is aseptic it gradually distends with mucus, and forms *mucocoele*, a thin walled, almost transparent sac containing many ounces of clear fluid.

If, on the other hand the content of the gallbladder is infected, acute obstructive cholecystitis develops. Inflammatory changes then proceed apace both in the tissue of the wall and in the lumen. The gall bladder becomes distended and greatly congested, its wall becomes thick, fleshy, and œdematous, the mucous membrane becomes swollen, ulcerated and perhaps gangrenous, and pus is exuded into the lumen—*empyema* of the gall bladder.

If, as usually happens, this acute phase subsides, as the œdema diminishes, the impacted stone loosens or any other obstructing agent is relieved, and the patency of the cystic duct may once again be restored. Probably the gall bladder never returns completely to the *status quo ante*, but assumes a state of chronic inflammation, often interrupted later by acute or subacute exacerbations.

Although this is the usual course, it sometimes happens that the disease progresses to further complications, and the infection, hitherto practically limited to the gall bladder, spreads more widely. Gangrene of the gall bladder wall may occur and lead either to sudden perforation into the general peritoneal cavity or, more commonly, to local abscess formation. As a further event, abscesses may form in the subphrenic space.

Perforation of the gall bladder may result also

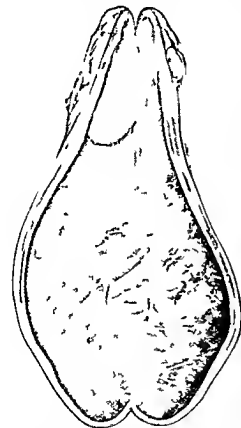


FIG. 254. Obstructive cholecystitis. The gall bladder thickened and scarred by chronic cholecystitis has become the seat of an acute infection following the impaction of a cholesterol stone near the cystic duct. The wall of the gall bladder is acutely congested and its mucous membrane is eroded. At the time of operation the gall bladder contained muco-pus.

from the direct pressure of a stone in the lumen, and in such a case it is usually situated over a stone impacted close to the cystic duct. A fistula may form between the gall bladder and other structures, especially the common duct or the duodenum, or, rarely, the colon or stomach. Such a fistula may allow the passage of a large stone into the intestines, and this may subsequently give rise to *gall-stone ileus*.



### Bacteriology of Cholecystitis

The infecting organisms in chronic cholecystitis include *B. coli* and non hæmolytic streptococci with occasionally, *B. typhosus* and *Cl. Welchii* and other bacteria. Similar flora may occur in acute cholecystitis though in this phase of the disease *B. coli* is by far the most common.

Much attention has been paid to the route by which the infecting organisms reach the gallbladder. Bacteriological investigations show that in chronic disease the organism can be recovered from the gall bladder wall more often than the bile and this has been taken as evidence that infection results from blood borne organisms reaching the gall bladder via the cystic artery. It seems much more likely however that the usual route of infection is by way of the bile. It is known that in chronic abdominal infections and even in simple constipation organisms gain access to the portal blood stream and thus to the liver whence they escape into the bile and the character of the bacterial flora in cholecystitis would seem to give support to the view that this is the important avenue of infection.

The common finding that the bile in diseased gall bladders is sterile can readily be explained for the bile is constantly flushed out and replaced and moreover it has a mild inhibiting effect on the growth of organisms.

### Course and Complications of Cholecystitis

As has already been indicated cholecystitis generally arises insidiously and pursues a chronic course. If no stones are present or if the stones lie freely in the lumen of the gall bladder no secondary pathological effects are produced and apart from attacks of pain the disease causes little or no impairment of health.

When however a stone impacts at the neck of the gall bladder or traverses the cystic duct it may give rise to a variety of complications.

Acute cholecystitis has already been described. As a complication of the acute infection local abscesses may form in the vicinity of the gall bladder or the subphrenic space. Acute perforation of the gall bladder into the general peritoneal cavity is a rare but dangerous event leading as it does to a severe type of biliary peritonitis (qv). It is interesting to note that though acute cholecystitis resembles acute appendicitis in its pathogenesis rupture of the gall bladder is far less common than rupture of the appendix owing no doubt to the toughness of the gall bladder wall to the low virulence of the infecting organisms and to the ease with which the omentum circumscribes it. When



FIG. 255. Hour glass gall bladder containing stones. The stones are of pure pigment type.

rupture of the gall bladder does occur the fundus is the common site, for this point is most distant from its blood supply.

Long standing pressure by a stone lodged at the neck of the gall bladder may lead to ulceration of the gall bladder wall and ultimately to the development of a fistula into the duodenum, whence a stone may pass into the distal part of the small intestine and there give rise to intestinal obstruction (wall stone ileus *see* p. 564). Less often a stone may ulcerate through into the colon and be evacuated per anum. In rare cases chronic perforation of the gall bladder may lead ultimately to the development of a fistula at the umbilicus, through which bile and stones may periodically be discharged.

The chronic irritation caused by a stone impacted in the gall bladder may eventually give rise to carcinoma of the gall bladder. Rarely as an end result of obstruction combined with chronic infection the gall bladder may undergo calcification (*see* p. 569).

### CHOLESTEROSIS OF THE GALL-BLADDER

(Strawberry Gall bladder)

This disease is by no means uncommon, but until recent years its frequency has not been fully realized. Its characteristic feature lies

in the deposition of large amounts of esters of cholesterol and other fat like substances in the mucous membrane where they form either multiple small yellow specks like the seeds of a ripe strawberry—*strawberry or fish scale gall-bladder*—or larger pedunculated masses known as *lipoid polypi*. When the gall bladder is opened and viewed from its inner aspect, the appearance is striking. In the normal organ the mucosa is raised into delicate ridges or villi. In the "strawberry" condition these ridges instead of being thin and tenuous are stout and swollen, distended by yellow lipoid masses. In severe



FIG. 254. Cholesterosis of the gall bladder. There are numerous massive deposits of cholesterol esters in the mucous membrane. Near the fundus there is a small lipoid polypus. Note that there are no cholesterol deposits in the cystic and common ducts.

examples the ridges throughout practically the whole gall bladder may be thus affected, and rarely even the intervening recesses also are invaded. Even when most extensive, however, the change is strictly limited to the gall bladder itself, and stops short often in a transverse yellow line, near the commencement of the cystic duct. The cystic duct and the common and hepatic ducts are never affected. *Lipoid polypi* are localized deposits of a similar nature, which enlarge and thus become pedunculated. They are usually single, but as many as a dozen may be present, often associated also with some degree of "strawberry" change.

Microscopically, the characteristic changes are confined to the mucous membrane, and the other coats may either be healthy or show merely the signs

of chronic inflammation. The ridges or villi of the mucosa, normally delicate tenacious folds, are prominent and swollen with lipoid material so that they have been said to resemble balloons, attached to the subjacent walls by delicate stalks. The great mass of the lipoid is contained in large cells which lie in the stroma of the mucous membrane, principally in clumps close to the tips of the villi. These lipoid containing cells closely resemble the charac-

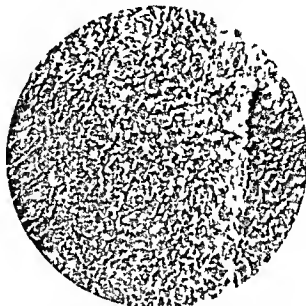


FIG 257 Cholesterosis of the gall bladder. Massive deposits of cholesterol esters are seen in the prominent ridges of the mucous membrane.

(Department of Surgery, University of Edinburgh)

teristic cells of subcutaneous xanthoma. The cell nucleus is small and stains deeply, and surrounding it is a very delicate cytoplasmic network in the meshes of which the lipoid collects. From their appearance these cells are known as "foamy cells." It is believed that they are of endothelial origin and are engaged in phagocytosis of the cholesterol.

Not infrequently cholesterol is deposited also in the columnar epithelial cells of the mucosa in the form of large globules near the basal aspect of the cells. When these are stained with Scharlach II or similar dyes a striking appearance is produced, as of a scarlet margin to the section.

**Pathogenesis.** It has often been stated that cholesterosis is a variety of cholecystitis, but this view cannot be accepted, for although the two conditions are often associated, cholesterosis may occur alone, with no trace of inflammatory change. Nor can cholesterosis be due,

as has sometimes been suggested, to a mere excess of cholesterol in the blood, for the blood cholesterol index is sometimes normal or even low.

From the strict localization of the cholesterol deposits to the gall bladder itself and their entire absence from the ducts, it seems clear that the disease is closely related to the function of the gall bladder in regard to cholesterol metabolism, but, in spite of much work, our knowledge of this function is not yet complete. It is known that the bile as it leaves the liver contains much cholesterol, which is either built up by the liver cells or derived from cholesterol in the blood, but it has been

found difficult to prove whether the gall bladder adds further cholesterol or, on the contrary, subtracts some from the bile.

At present there are two main views in regard to the origin of cholesterosis. The first is that the cholesterol is deposited directly from the blood stream, as a result of breakdown of a cholesterol-secreting mechanism in the gall bladder. The second view, more widely held, is based upon the belief that normally cholesterol is subtracted from the bile in the gall bladder, but only to a very moderate



FIG. 258 Cholesterosis of the gall bladder. Paraffin section of a villus of the mucous membrane. The villus is distended by numerous foamy cells with small nuclei and delicate reticulate protoplasm in the meshes of which the cholesterol is held.

(Department of Surgery, University of Edinburgh.)

extent unless the bile cholesterol concentration is high. In health the absorbed cholesterol is probably combined with other substances which render it 'masked' and invisible, and is then transported rapidly into the blood stream. According to this view cholesterosis is thought to result from two processes (1) increased absorption of cholesterol from the bile through the gall bladder wall due to a high bile cholesterol content, and (2) an alteration in the physical or chemical state of the absorbed cholesterol, which renders it visible, prevents its further transport, and leads to its aggregation in large masses.

**Relation to Cholecystitis.** It is generally believed that cholesterosis is in some way due to cholecystitis, and it has been suggested that the cholesterol deposition results from inflammatory fibrosis and obstruction of the lymph channels by which the cholesterol is normally carried away. Cholesterosis may occur, however, in an otherwise healthy gall bladder, although in most examples removed by operations it is accompanied by mild inflammatory change. Moreover, cultures from straw

berry gall bladders are sterile in a large proportion of cases. These facts seem to justify the view that primarily cholesterosis may be an aseptic process. It is possible, however, that cholesterosis renders the gall-bladder liable to infection.

**Relation to Gall-stones.** Cholesterosis may occur with or without gall stones. Stones were present in 17 of a series of 35 cases recently

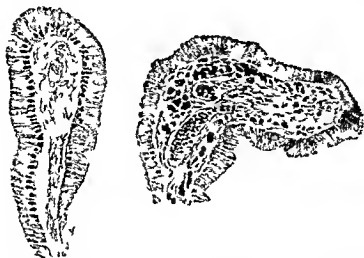


FIG. 259. Two villi from a strawberry gall bladder. (Frozen section stained by Scharlach R.) Cholesterol deposits (left) in the basal parts of the epithelial cells and (right) in foamy cells in the stroma.

(Department of Surgery University of Edinburgh)

examined. It is a striking fact that the stones are commonly of pure cholesterol type. In the series referred to, no fewer than eleven of seventeen stones were of this type, a frequency out of all proportion to their general incidence. The nature of the relationship is considered in the section on gall stones.

### CALCIFICATION OF THE GALL-BLADDER

This rare condition is characterized by deposition of calcium in the outer (muscular and subserous) coats of the gall bladder, either in patchy fashion or throughout the viscus. To outward appearance, the gall bladder is pale, smooth and shiny, sometimes resembling porcelain. On its inner aspect, the wall is irregular and rough, for the mucous membrane, deprived of its blood supply, generally sloughs.

Calcification of the gall bladder is almost always a late sequel to calculous cholecystitis. In most cases the gall bladder is of large size, is thick-walled and contains a stone impacted in or close to the cystic duct, and it is obvious that the calcification has supervened upon a chronic obstructive cholecystitis with empyema of the gall bladder. In addition to the primary obstructing stone the gall bladder may contain secondary stones composed of calcium carbonate, and also thick, gritty debris rich in calcium. In other cases a calcified gall

bladder is of small size, tightly contracted round a large stone or a number of closely packed faceted stones

The disease occurs principally in elderly females. It is remarkable that in the majority of cases the symptoms are slight or even absent. The condition may be recognized by the discovery of a painless, mobile, stony hard lump in the right hypochondrium whose outline is obvious radiographically.

### VOLVULUS OF THE GALL-BLADDER

A gall bladder which has an abnormally loose attachment to the liver by a complete mesentery may undergo torsion. Rotation may be clockwise or anti-clockwise, and may be through a full circle. The few cases reported have occurred chiefly in elderly women and in gall bladders which in other respects had been healthy. In most cases there have been no calculi, and no constant predisposing factor has been observed.

Torsion occurs acutely and is associated with severe pain and shock. It leads to interference with the blood supply and is followed by gangrene and perforation of the gall bladder.

### TUMOURS OF THE GALL-BLADDER

**Simple Tumours** Simple tumours of the gall bladder are not uncommon, but from their small size and innocent nature they are often not recognized. Occasionally a benign *adenoma*, composed of columnar cells arranged in acini, is found near the fundus of the gall bladder forming a button like prominence in the wall. A true *papilloma* is rare. *Lipoid papilloma* is the name sometimes given to the cholesterol laden polypi of cholesterosis, but these are merely due to the aggregation of cholesterol in the villi, and are not to be regarded as tumours. True papillomata contain no lipoid material, but form small greenish projections on the mucous surface. Microscopically they have the character of papillary adenomata, with acini of columnar cells set in a well formed stroma. Rarely such papillomata may be multiple covering the whole surface of the gall bladder, and in such cases they must be regarded as potentially malignant.

**Malignant Tumours** Carcinoma is practically the only malignant tumour of the gall bladder, although there are a few reported cases of sarcoma, melanoma and endothelioma, and one case which resembled a hypernephroma.

Carcinoma of the gall bladder is now known to be far from rare. It is found in from 1% to 2.5% of surgical operations on the biliary tract, and comprises 2% to 5% of all cases of malignant disease seen at autopsy. It is most common in women between the ages of fifty and sixty five years.

The tumour is of special interest as one of the most striking examples of malignant disease developing as a sequel to chronic irritation, for it is almost invariably an end result of chronic cholecystitis, in most cases accompanied by gall stones. There are many cases on record,

moreover of carcinoma developing months or even years after operative removal of the stones

Carcinoma of the gall bladder spreads at an early stage beyond the confines of the gall bladder and soon oversteps the limits of successful removal. It invades the liver by direct continuity forming a large mass sometimes 8 or 10 cm. in diameter at its lower border. It spreads to the lymph glands along the cystic and common ducts and thus may

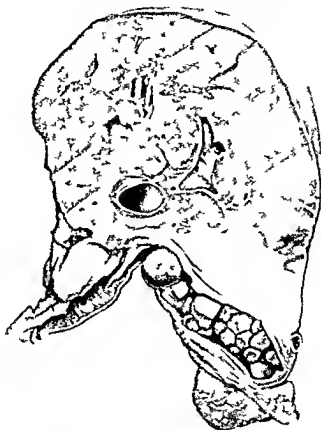


FIG. 260. Carcinoma of the gall bladder invading the liver. The tumour of scirrhous character has caused a diffuse thickening of the gall bladder and forms an ill-defined pale mass infiltrating the liver. There is a large secondary growth in the cystic lymph gland. Note the association of gall stones and carcinoma.

(Department of Surgery, University of Edinburgh.)

cause obstructive jaundice. In some cases it disseminates through the peritoneal cavity. Distant metastases are uncommon except in the lungs but there are a few cases on record of secondary growths in bones and even in the breast.

Four types of carcinoma of the gall bladder may be recognized. (1) The *scirrhous carcinoma* is the commonest. It is a columnar-cell adenocarcinoma with an acinar structure and a dense fibrous stroma and it gives rise to a very hard growth which infiltrates the gall bladder wall. At an early stage it forms a localized induration which may be



FIG 261 Papillary adenocarcinoma of the gall bladder In places there are irregular glandular acini whereas in other parts there is a definite papillary formation

mistaken for an area of chronic cholecystitis In some cases it encircles and obstructs the cystic duct and may predispose to the development



FIG 262 Adenocarcinoma of the gall bladder invading the liver The columnar cells of the tumour (below) are arranged in irregular acini The liver cells bordering on the tumour (top right) are flattened and atrophied and those a little further away show various degrees of fatty degeneration

of empyema of the gall bladder or if it arises near the midpoint of the viscus it may give rise to an hour glass deformity Ultimately, in most cases it completely envelops the gall bladder and almost obliterates the lumen



(2) *Papillary or proliferative carcinoma* is less common. It is an adenocarcinoma with a scanty stroma. The cells, columnar in shape, are arranged in irregular acini and may show a papillary arrangement. The growth is soft and often bulky, and tends to project into and fill the lumen of the gall bladder.

(3) *Colloid carcinoma* is a soft tumour, recognizable by its gelatinous character. Sometimes the whole tumour is of colloid type, sometimes only a part is affected, and in some the condition is recognized only on microscopic examination. The cells, few in number, lie singly or in ill formed acini, whilst the bulk of the tumour is made up of a structureless, blue staining material, pseudomucin. The cells contain droplets of this substance in their cytoplasm, and some of them are distended to signet ring shape.

(4) *Squamous carcinoma (epithelioma)* is a rare form of tumour, which presents characters similar to carcinoma of such squamous cell membranes as the skin, the tongue or the œsophagus. The cells are of squamous type, there may be cell nests or epithelial pearls, and it is sometimes possible to identify typical prickly cells with intercellular bridges.

In some cases the whole tumour is of this type, in others only a part shows the squamous character, and there is a confusing appearance of areas of squamous epithelioma adjoining and merging into areas of columnar cell adenocarcinoma.

Squamous epithelioma of the gall bladder is generally regarded as an example of metaplasia, and it is thought possible that the growth arises in an area of the mucosa affected by leukoplakia as a result of the chronic irritation of gall stones. Nicholson has pointed out that the development of squamous cells in a viscus of entodermal origin such as the gall bladder has its analogy in the normal development of the œsophagus, which, like the rest of the foregut, is originally lined by columnar cells, but develops a squamous cell membrane at an early stage of embryonic life.

## ABSCESSSES IN THE LIVER

**Solitary Abscess.** Almost always this is a *tropical abscess* following amœbic dysentery, but in rare circumstances a single abscess may arise from other causes, as from the spread of infection from the gall-bladder, or from suppuration in a hydatid cyst, or from pyæmic infection.

A tropical abscess results from infection of the liver by amœbæ, which presumably reach this situation *via* the portal blood stream. The disease affects Europeans living in the tropics with relatively greater frequency than the indigenous, and occasionally it has affected persons who have never visited the tropics. In 60% to 80% of cases the abscess develops in the right lobe of the liver, and often near its superior surface. It may attain large size, and is rarely recognized until several ounces of pus have collected. Rarely it may hold as much as 10 pints. The wall of the abscess is composed of necrotic liver tissue,

and is usually shaggy and irregular. Later, much fibrous tissue develops and may form a fairly well defined capsule.

The pus may be of creamy appearance, but is usually chocolate coloured from degenerating liver substance, and is often viscid and glairy. Amœbæ are present in the wall and adjacent liver tissue, but are often difficult to demonstrate.

Secondary perihepatitis usually develops, and the liver becomes fixed by adhesions to the diaphragm, abdominal wall and viscera. For this reason, downward displacement of the liver is unusual and the full extent of the enlargement is evidenced by radiographic demonstration of elevation of the diaphragm. The abscess may remain intact but often it ruptures, especially into the lung, pleura or peritoneum. Superadded infection with pyogenic organisms may occur.

#### Multiple Abscesses

(1) *Pyæmic Abscesses* These may occur in the course of any general pyæmia. They are scattered through all parts of the liver and are of small size, and as the liver affection is generally overshadowed by the severity of the general disease, they have little clinical significance.

(2) *Abscesses from Pylephlebitis and Portal Pyæmia* Suppurative pylephlebitis results most often from appendicular infection, occasionally from suppurating lesions in the pelvis, e.g., salpingitis, suppurating ovarian cysts, or even infected hæmorrhoids, and rarely from other intra abdominal diseases. Males are affected most often, and most cases occur in the third decade. The disease follows infective thrombosis of the vessels near the original lesion, e.g., the appendicular veins, and from here it may extend to any part of the portal venous system, sometimes principally involving the extrahepatic vessels, sometimes the intrahepatic ones. The portal vein and its branches contain brownish pus mixed with breaking down blood clot, their walls are swollen and acutely inflamed, and the perivascular tissues may also suppurate.

The liver is enlarged and tender. Its surface may be smooth, or



FIG. 263 Multiple abscesses in the liver, due to pylephlebitis.  
(Museum of Royal College of Surgeons of Edinburgh.)

nodular with numerous projecting abscesses, and it is usually adherent to the diaphragm and parietes. When cut it is seen to contain numerous abscesses, varying up to the size of walnuts, and between the cavities are pale yellow areas where the liver has undergone necrosis. Usually the abscesses are scattered through all parts of the liver, but sometimes one lobe, especially the right, may be more affected, a localization which probably depends in part upon the fact that the portal blood stream runs in currents, so that the blood from any one organ remains more or less separate and is diverted principally towards one or other lobe. Fortunately, the disease is very rare, for it almost invariably proves fatal, often from spread of the infection to the lung, pleura or peritoneum.

*Portal pyæmia* is the term used for a similar condition in which the abscesses are believed to be due to infected emboli in the portal stream rather than to direct infection along the vessel walls. It presents no distinctive features, however, and the two conditions are generally regarded as one.

(3) *Cholangitic Abscesses*. As the name indicates these abscesses follow infection of the liver secondary to cholangitis, and consequently they are usually due to a gall stone in the common duct. Rarely they result from other lesions associated with stagnation of the bile, such as the pressure of a tumour or, in the East, the presence of liver flukes or worms.

The liver is enlarged, and scattered through it are numerous greenish yellow areas. Some of these are soft, but others are solid and may even resemble secondary malignant nodules. Sometimes the abscesses lie near the surface of the liver, and adjacent cavities may become confluent and reach larger size. The cavities communicate with bile ducts, into which they discharge their contents, and consequently the pus is deeply bile coloured, and often mixed with "biliary mud."

Clinically, abscesses of this type are associated with the syndrome "Charcot's intermittent hepatic fever." Jaundice develops, of a peculiar ashy grey type. The enlarged liver becomes tender and painful, the temperature swings intermittently, with frequent rigors, and there is severe toxæmia with sweating and rapid loss of weight.

## CYSTS OF THE LIVER

There are two principal types of liver cyst, the parasitic and non parasitic.

*Parasitic cysts* occur in hydatid disease, and the liver is the commonest site of this affection (see p. 50). Usually there is a single cyst, but occasionally multiple cysts are present. Hydatid cysts are most common in the right lobe of the liver, and, according to Dew, they are situated towards its inferior aspect in 75% of cases. Consequently they tend to project towards the peritoneal cavity and become palpable through the abdominal wall. The cyst may be unilocular and contain no daughter cysts, but more often these are present, often in considerable numbers. Sometimes the cysts attain large size. They may rupture into the peritoneal cavity, into the biliary passages or the stomach, or

through the diaphragm but the commonest termination is calcification. Occasionally superadded septic infection of the cyst occurs.

*Non parasitic cysts* are not uncommon, but being generally symptomless they rarely demand surgical attention. Three main types are recognized.

(1) *Cysts associated with polycystic disease of the kidneys* are nearly always multiple. The liver is greatly enlarged and under its capsule project numerous cysts containing clear watery or blood-stained fluid. The cysts are of congenital origin but may be of small size at birth and generally remain unrecognized until adult life or even old age. They are said to be three times commoner in females than in males. Their mode of origin is not fully understood but it seems probable that they are formed by the irregular proliferation of aberrant hypoblastic cells arising from the primitive biliary papilla.

(2) *Cysts associated with tumours* are seen in cystic adenoma of the liver and occasionally in bile-duct carcinoma and other growths. There are one or two cases on record of teratomatous (dermoid) cyst.

(3) *Retention cysts* are generally solitary, or there may be a number of small cysts communicating with one large cavity. The cyst has a wall of fibrous tissue often lined by a single layer of flattened epithelium and it contains watery fluid, straw-coloured or sometimes blood-stained. The cyst does not communicate with the biliary system and therefore does not contain bile. Cysts of this type are generally regarded as due to retention within a small bile duct, the result of local obstruction by fibrosis. In most cases the cyst is small and gives rise to no symptoms unless hæmorrhage occurs when acute pain and fever may result. Occasionally a cyst reaches large size, and may contain as much as 12 pints of fluid. It may then exert pressure on neighbouring structures the stomach duodenum portal vein inferior vena cava or even the right ureter.

### GUMMA OF THE LIVER

The liver may be affected in inherited syphilis or in the secondary or tertiary stages of acquired syphilis. From the surgical standpoint it is only necessary to consider the gumma of tertiary acquired disease.

Gummata are usually multiple, and occur principally near the surface of the liver under the capsule. They may be scattered in different parts of the liver but usually the right lobe is particularly affected. In appearance and microscopic characters they do not differ from gummata elsewhere. They vary in size up to several centimetres in diameter, and are composed of dense fibrous tissue often somewhat necrotic at the centre. Microscopically, it is seen that the smaller gummata lie in the capsule of the liver and in its prolongations in the portal tracts. Surrounding the central necrotic portion is a well-developed zone of fibrous tissue with areas of lymphocytic infiltration. Endarteritis obliterans is usually a striking feature in the adjacent blood vessels.

Gummata of the liver are of special importance surgically, owing to their tendency to mimic other biliary diseases. To the naked eye they are often indistinguishable from secondary malignant growths.

and such confusion is all the more likely since the subjects of hepatic syphilis are often emaciated and cachectic. Gummata of the liver may simulate cholecystitis, for they may give rise to irregular fever and intermittent attacks of jaundice. Healing of a gumma is accompanied by extreme scarring, and this may cause obstructive jaundice and mimic the effects of a tumour of the common duct or of the pancreas.

### ACTINOMYCOSIS OF THE LIVER

This is a rare affection, and is almost always secondary to actinomycotic disease of the intestinal tract. The lesions have the characteristics of actinomycosis elsewhere (*see p. 47*). The abscess is usually multilocular, and on section has the appearance of a honeycomb of yellow colour. The liver becomes adherent to the diaphragm or to the abdominal wall, and the abscess may rupture into the lung, into the stomach, or on the skin surface, especially after superadded infection.

### PRIMARY TUMOURS OF THE LIVER

**Simple Tumours.** *Adenoma and angioma* are uncommon, and usually have little clinical importance. They may grow to large size, and may then cause symptoms from pressure. When situated near the inferior margin of the liver such a tumour may become pedunculated, forming an obvious mobile intraperitoneal swelling of considerable size.

#### Primary Malignant Tumours

Carcinoma may arise either from the liver cells or from the epithelium of the smaller bile ducts. Sarcoma also occurs. All varieties are rare, and every case requires critical observation to determine that it is not secondary to an obscure primary tumour. *Primary liver cell cancer* is of interest, in that it is usually associated with cirrhosis or subacute atrophy of the liver. In these diseases a striking feature is the great regeneration of liver cells, and it appears that cancer arises when this process gets out of control, and when the proliferating liver cells throw off all restraining influences. The growth forms a large mass of soft solid tissue, very liable to undergo necrosis and softening. Usually the mass is single, but numerous secondary nodules develop in the rest of the liver. Metastases rarely appear in other organs. Microscopically, there are rounded masses of liver cells, which show irregular mitotic figures and other evidence of rapid growth.

Cancer arising in the intrahepatic bile ducts may closely resemble liver cell cancer. There is, however, usually no cirrhosis. The liver is enlarged and contains multiple nodules, each having the structure of a columnar cell adenocarcinoma.

### SECONDARY TUMOURS IN THE LIVER

The liver is more often affected by secondary tumours than any other viscus, and secondary tumours are very much more common than primary growths.

In the majority of cases the liver is involved by metastases derived from tumours within the portal area, and especially by carcinoma.

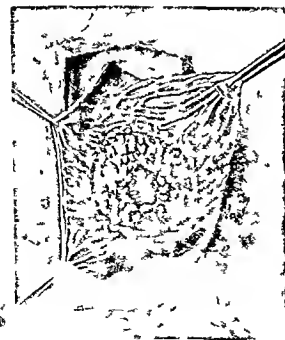
of the stomach the colon or the lower end of the oesophagus in that order of relative frequency. Secondary growths from these three regions constitute about 50% of liver tumours. Less commonly the liver is involved by carcinoma of the gall bladder pancreas lung breast and kidney and by sarcoma originating in other parts of the body.

As a rule secondary growths are multiple and are scattered in all parts of the liver but sometimes a solitary metastasis may attain considerable size before others appear. Occasionally one lobe of the liver is affected to a much greater extent than the remainder of the organ.

Small secondary nodules are usually of firm consistency and are much harder than the surrounding liver tissue through which they can readily be felt. As they increase in size the central parts deprived of their blood supply undergo degenerative changes and become softened hence large metastases are often umbilicated. The growths are usually of pale colour and sometimes pearly white but occasionally especially when of rapid growth they are vascular and deep red. The natural features of such tumours as melanoma and chorionic carcinoma are usually reproduced in the metastases.

### TUMOURS OF THE BILE DUCTS

The only bile-duct tumour in man is a *carcinoma* which may arise from either the intrahepatic or the extrahepatic ducts. It is commoner in males than females and occurs usually in later life.



carcinoma of the Ampulla of Vater

In the extrahepatic ducts the growth commonly arises either in the region of the duodenal ampulla or at the junction of the cystic with the common ducts. It forms a rounded hard swelling rarely larger than a cherry leading to a stricture and to complete obstruction of the duct. Death from obstructive jaundice usually occurs before the tumour metastasizes. Microscopically it has the structure of a columnar cell adenocarcinoma.

If the growth is in the cystic duct the gall bladder unless fibrous from stitis becomes distended and if the growth lies above

the level of the cystic duct the gall bladder will be small or empty. At operation the great difficulty is to distinguish a small growth from a fibrous mass around a stone. If, as commonly happens, the growth is small and in the lower part of the duct it may readily be overlooked.

Carcinoma of the intrahepatic bile ducts frequently takes the form of multiple small pale nodules which appear to arise simultaneously. It is distinguished with some difficulty from a primary liver cell cancer, from which it differs in that it has columnar cells arranged round a definite lumen.

### CYSTIC DILATATION OF THE COMMON BILE DUCT

This is a rare congenital abnormality which rarely comes to light until adolescence. It affects females four times more commonly than males. There is a dilatation like a saccular aneurysm, which is connected with the supraduodenal part of the common duct and forms a cystic swelling of variable size, sometimes as large as a man's head. As the cyst enlarges it stretches the duct system so that the hepatic ducts may open separately into the cyst above, and the common duct leaves it lower down. The cystic duct also may have a separate opening. The ducts above and below the cyst may be of normal calibre, but they are often dilated and tortuous, and the liver may be cirrhotic. The wall of the cyst in some cases is thin and translucent transmitting the greenish colour of the bile, in others it is thick and fibrous, and may be studded with large calcified plaques and ulcers. The biliary content may be clear, or may be of the consistency of pea soup. There is usually no lining membrane, but there may be a layer of columnar cells, and even exceptionally squamous epithelium (Wilkie). As the cyst enlarges it follows the line of least resistance, and this is usually downwards and to the right, so that it raises the posterior parietal peritoneum of the right subhepatic fossa. The duodenum may be displaced downwards or may be stretched across the front of the cyst, and the right colic flexure displaced downwards and medially. Morley has described a case in which downward displacement of the small intestine stretched and constricted the root of the mesentery and gave rise to secondary duodenal ileus. The cyst may periodically become dilated, when it tends to kink and obstruct the common duct. Infection by coliform bacilli is a frequent complication and may prove fatal.

The diagnosis of a cyst of the common bile duct is suggested by the presence of a large cystic mass in the right hypochondrium occurring in an adolescent girl and accompanied by recurring abdominal pain, intermittent jaundice, and sometimes fever.

### JAUNDICE

Jaundice is the state characterized by an excess of bile pigment in the circulating blood and the tissues. Three types of jaundice are recognized —

- (1) Haemolytic, exemplified in "acholuric jaundice" and other

diseases of the spleen and reticulo-endothelial system. In these cases there is a simple excess of pigment, due to excessive destruction of the red blood cells. (2) Toxic infective, for example, catarrhal jaundice and the jaundice due to metallic poisons. Here the main feature is degeneration of the polygonal cells of the liver. (3) Obstructive, as in occlusion of the bile ducts by stone or neoplasm. Here the bile, after being excreted, is reabsorbed from the ducts into the blood stream.

**Obstructive Jaundice.** From the surgical standpoint obstructive jaundice is the most important type, and its pathological features will be considered more fully. Obstructive jaundice may be caused by (1) foreign bodies within the common duct, such as stones or, rarely, parasites. (2) lesions of the common duct, such as carcinoma or, rarely, fibrous structure, (3) lesions compressing the common duct from without, such as carcinoma of the pancreas, secondary neoplasms, and rarely tuberculous or lymphadenomatous glands in the hilum of the liver.

Jaundice develops rapidly after the onset of obstruction to the biliary outflow, and may be evident by yellowness of the conjunctiva within a few hours. Then the skin becomes pigmented and the urine discoloured and finally nearly every tissue is affected. The only unpigmented substances are certain secretions such as the saliva, the secretion of the common duct, and usually the milk and cerebrospinal fluid.

At first jaundice is slight, and the colour of the skin is light yellow, but in complete obstruction of long standing it deepens to an olive hue (black jaundice) owing to oxidation of the bilirubin to biliverdin. If cholangitis and intrahepatic suppuration follow, with toxæmia and cachexia, the colour turns to a sickly greenish grey (grey jaundice).

**Effects of Obstructive Jaundice.** The effects of obstructive jaundice may be classified under four headings—

- (1) Retention of the bile constituents
- (2) Dilatation of the biliary system
- (3) Impairment of liver function
- (4) Alteration in blood coagulability

(1) *Retention of the Bile Constituents.* All the bile constituents are retained and may show an increase, temporary or permanent, in the blood. The bilirubin content of the blood rises from the normal of about 1 mg. to as much as 250 mg. per litre. Correspondingly, the icteric index may rise from the normal figure of 5 to over 200 units. If the jaundice continues during several weeks, the bilirubin content may finally show a slight decrease.

The bile salt content of the blood is also increased and the cholesterol content of the blood may rise from the normal of about 150 mg. % to double that level. This is not, however, an invariable feature, and the blood cholesterol may remain within normal limits.

It is interesting to note that few of the pathological effects of jaundice can be ascribed to retention of the bile constituents. The bile salts are the only toxic constituents, but in most cases their increase in the blood is only transient. The bile pigments have been shown to be completely non-toxic even when present in large amount, whilst



the cholesterol increase is no greater than may occur, for example, in pregnancy

(2) *Dilatation of the Biliary System* The first effect of obstruction is to raise the pressure within the whole biliary tract, and to distend the whole duct system, including all the fine biliary radicles within the liver (hydrohepatosis). This dilatation is usually most extreme when due to carcinoma, for infection is then often lacking and the ducts are thin walled, whereas when stones are present there is usually infection and the ducts are thickened by fibrosis. The gall bladder similarly is usually dilated when carcinoma is present, contracted by fibrous tissue when the obstruction is due to stones (Courvoisier's Law), but since carcinoma and stones may coexist this is by no means a dependable criterion.

If the obstruction is maintained a striking alteration occurs in the content of the duct system, and the bile becomes pale and colourless (white bile). When the pressure in the biliary tract reaches approximately 300 mm. of water, the liver is unable to continue its excretory function, and bile production ceases. The small glands in the walls of the common and hepatic ducts, which normally secrete a little clear fluid, are able to withstand a considerably higher pressure than this, and they continue to function, so that gradually the stagnant bile is replaced by their secretion. This is the so called "white bile," a clear, watery, slightly alkaline fluid containing a trace of mucin, but no other bile constituent and no pigment. It is a striking feature as Wilkie commented, that in a patient deeply jaundiced one of the few uncoloured substances in the body is this fluid in the common bile duct.

If the gall bladder is absent or functionless through disease, this state of affairs is reached within a week from the onset of complete obstruction. On the other hand, a functioning gall bladder delays the appearance of white bile for a much longer period. Sometimes when a healthy gall bladder is present an intermediate stage is found. The gall bladder contains green bile, but the content of the ducts is colourless.

(3) *Impairment of Liver Function* Impairment of liver function constitutes one of the major dangers after operation upon cases of obstructive jaundice. The impairment is due partly to "back pressure" within the distended bile radicles, which leads to atrophy of the liver cells, partly, in some cases, to coincident infection. Thus we find evidence of liver dysfunction most marked in prolonged jaundice and when cholangitis is present—the latter a common occurrence in cases of stone in the common duct.

The liver function most obviously affected is glycogen storage, and the special risk of operation in obstructive jaundice arises from the fact that this is also the function most gravely affected by operative trauma and by certain anaesthetics. In some cases, the impairment of glycogen storage can be demonstrated by the levulose tolerance test.

In the late stages of severe obstructive jaundice, all the manifold functions of the liver may suffer to some degree. The metabolism of fats and proteins is upset, *poisonous* nitrogenous products, which are normally converted by the liver into urea, remain in the circulation unchanged and cause secondary *toxic* effects upon the heart, kidneys

and other organs, the alkali reserve of the blood is reduced, and eventually there supervenes a state of cholemia, which closely resembles uremia.

(4) *Alteration in Blood Coagulability* It is well established that in obstructive jaundice there is a definite tendency towards hæmorrhages. This tendency is most noticeable in the late stages of deep jaundice due to malignant obstruction of the common duct, and it constitutes one of the major risks of operation. Indeed, it has been stated that 50% of post operative deaths in jaundice are due to this cause. The bleeding takes the form of an ooze from any incised or traumatized surface, and often leads to the formation of a hæmatoma in the depths of the wound.

It is remarkable that hæmorrhages are rare in cases not submitted to operation. It seems as though the trauma of the operation, or the added liver damage, or perhaps the sudden biliary decompression, in some way increases the risk of bleeding in the post operative period.

It is now known that the bleeding tendency is due to a deficiency of prothrombin. Normally prothrombin is synthesized in the liver out of Vitamin K, which is derived from green food-stuffs or formed as a result of bacterial activity in the intestinal tract. In obstructive jaundice, owing to absence of bile from the intestine the vitamin, which is fat soluble, is not absorbed in adequate amount, and in addition its elaboration into prothrombin is impaired owing to liver damage.

Chemical investigations have shown that the vitamin is a member of the naphthoquinone series. Other naphthoquinones, notably 2 methyl 1 4 naphthoquinone, are equally active, and after intramuscular injection are effective in restoring the normal prothrombin level within a few hours.

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## CHAPTER XXIX

### DISEASES OF THE PANCREAS

#### ACUTE PANCREATITIS (Acute Necrosis of the Pancreas)

ACUTE pancreatitis is one of the gravest of all acute abdominal diseases. It exceeds even perforation of a peptic ulcer in the sudden and dramatic illness it causes, the pain to which it gives rise is more agonizing, the patient's strength is depleted with greater rapidity, and shock and toxæmia are of earlier appearance and are more pronounced. In fulminating cases the mortality is about 50%, whilst in the less severe types the disability occasioned is severe and prolonged.

Acute pancreatitis is fortunately not very common. It affects males and females with about equal frequency and is most frequent between the ages of fifty and sixty years, though in exceptional cases it occurs much earlier.

#### Morbid Anatomy

The pathological changes in acute pancreatitis vary according to the intensity of the disease. Formerly it was the custom to describe three different types, hæmorrhagic, gangrenous and purulent, but this classification is somewhat misleading, in that gangrene or necrosis of the pancreas is an invariable feature, whilst hæmorrhage and suppuration are now regarded as secondary effects, varying in extent according to the intensity of the primary destructive change. In conformity with modern conceptions of the disease, therefore, it seems preferable to recognize two main varieties, the fulminating type, which is generally associated with hæmorrhages, and the subacute type, which may sometimes proceed to suppuration.

**Fulminating Pancreatic Necrosis.** In this type the disease originates with dramatic intensity and may bring about a fatal issue within two or three days. Operation or autopsy reveals extensive necrosis of the pancreas with hæmorrhages in the vicinity of the gland and a hæmorrhagic or turbid effusion into the peritoneal cavity, whilst spots of fat necrosis are seen in the extraperitoneal and omental tissues and in even more distant situations.

The pancreas is swollen and necrotic, soft and friable in consistency, purplish from extravasated blood or with a yellowish green tinge as a result of bile staining. In most fulminating cases the whole pancreas is involved, but occasionally the changes are limited to one portion of it. The connective tissues in the vicinity of the pancreas are tense with œdema or infiltrated with blood, whilst the adjacent peritoneal surfaces are deeply congested. Microscopically, the most conspicuous change is necrosis of the parenchyma and interlobular septa, with

hæmorrhages around the necrotic areas and in the surrounding areolar tissue. Evidence of an inflammatory reaction is notably lacking at this early stage and cultures usually prove sterile. Hyaline changes in the blood vessels are usual and there may be widespread thrombosis.

The hæmorrhages vary in extent, and in some cases are so great as to give the appearance of a diffuse retroperitoneal hæmatoma. Sometimes there are hæmorrhages also in other sites, for example in the abdominal wall, whilst occasionally the blood gravitates towards the loins and gives rise to discoloration of the skin in these regions.

The hæmorrhages are believed to occur as a result of degenerative changes brought about in the walls of blood vessels by enzymes liberated from the pancreas. Rich and Duff have drawn attention to a peculiar hyaline necrosis of the vessel walls, affecting particularly the muscle fibres of the media and the internal elastic lamina, and have shown that a similar lesion may be produced experimentally by the subcutaneous injection of trypsin.

*Fat necrosis* is one of the most characteristic changes in acute pancreatitis. It is most abundant in the neighbourhood of the pancreas but also occurs in the fat of the omentum, the transverse mesocolon and other extraperitoneal tissues or in the anterior abdominal wall. In these regions it has been attributed to the action of lipase liberated from the pancreas and permeating along lymph vessels. Rarely, fat necrosis has been observed in more distant sites, such as the bone marrow, possibly as a result of excessive amounts of lipase carried in the bloodstream.

In the vicinity of the pancreas the necrotic fat gives rise to greyish yellow sloughs of cheesy or putty like appearance. Elsewhere, the areas of necrosis take the form of small raised tallow like spots, of firm consistency and yellowish white colour. In these spots the neutral fats are saponified by lipase with the formation of glycerol and fatty acids, the latter form acicular crystals and may later combine with calcium to form insoluble soaps, which are deposited as globular masses and may reproduce the outline of the original cells. Eventually, if recovery occurs, these deposits may be reabsorbed.

The *biliary tract* often presents pathological changes in acute pancreatitis. Stones are found in the gall bladder with a frequency variously estimated at from 40% to 70%, and it is remarkable that the stones are commonly of small size, the size of split peas or smaller. In occasional cases a stone is found in the common bile duct or impacted at the duodenal papilla. The gall bladder may present slight chronic cholecystitis or be fibrous and contracted as a result of long standing inflammation. The bile is usually dark in colour, muddy or blood-stained, and culture may reveal the presence of *B. coli*, streptococci, or sometimes *B. welchii*.

**Subacute Pancreatic Necrosis.** Here the pathological process is the same, but the disease proceeds less urgently, and recovery is usual. At operation, the pancreas is swollen and presents a brawny induration (if cut into, it is seen to be occupied by numerous small solid white foci of necrosis), the retroperitoneal tissues are œdematous, and there are scattered spots of fat necrosis in the vicinity, but these changes are

less extensive than in the fulminating type and generally there are no hæmorrhages

In some cases the disease affects the whole pancreas in others only a small portion is necrotic and the secondary changes are correspondingly localized

In cases seen two or three weeks after the onset of the disease an abscess may be found either in the retroperitoneal tissues or more commonly in the lesser peritoneal sac. Such an abscess contains thin pus or turbid watery fluid and there may be large grey sloughs which probably consist of necrotic fat. The abscess is commonly sterile and is thought to result from an aseptic inflammatory reaction caused by the presence of necrotic tissue or by irritation of the peritoneum from escaped pancreatic ferments. It seems probable that the so-called false cyst of the pancreas (p. 583) often originates similarly as a result of a mild or localized pancreatic necrosis

### Ætiology

The intensity of the pathological process, the lack of histological evidence of inflammatory change in the fulminating cases and the negative bacteriological findings all point to the conclusion that the disease is not primarily due to bacterial infection. It is now generally accepted that the condition is essentially an acute necrosis of the pancreas and is due to destruction of the glandular acini by the digestive action of its own juice. The pancreas secretes three enzymes, trypsin, diastase and lipase, and it is to the activity of the first named that the auto-digestion is attributed. Normally the trypsin is secreted in an inert form (trypsinogen) and is activated in the duodenum by the enzyme enterokinase. It is clear therefore that the cause of acute pancreatic necrosis is to be found in a study of the conditions under which the trypsin may be activated whilst still within the pancreas.

In 1901 Opie of Johns Hopkins Hospital reported a case of pancreatic necrosis in which he found a small gall stone impacted at the duodenal papilla and gave strong support to the view that the activation of pancreatic juice is caused by a reflux of bile into the pancreatic duct. This bile reflux theory has since been the subject of great controversy and much interesting evidence has been collected both in favour of and against it.

It is well established that trypsinogen is activated by bile especially if infected and animal experimentation has shown that acute pancreatic necrosis can readily be produced by the injection of bile into the pancreatic duct. Trypsinogen can also be activated by many other agencies, including certain chemical substances and organisms such as *B. coli* but infected bile is far the most potent substance known and actually has a more powerful activating effect than enterokinase itself. It has been objected that experimental pancreatic necrosis can be produced only if the bile is injected under considerable pressure which may well cause rupture of the pancreatic acini and escape of secretion into the interlobular connective tissues but it may be observed that bile is normally secreted at the pressure of 30 to 40 cm.  $H_2O$  and that the biliary pressure may be raised as high as 100 cm. by a forceful con-

traction of the gall bladder. That mechanical rupture of the pancreatic acini is not the sole factor is shown by the observation that pancreatic necrosis cannot be produced by even forceful injection of bland substances.

Opie's suggestion that impaction of a gall stone at the duodenal papilla might be a common aetiological factor has not been borne out by experience. Thus it is found that whereas gall stones are commonly found in the gall bladder (40% to 70%) and are commonly of such a size as to be capable of being carried down and impacting at the papilla, the demonstration of such an impacted stone is rarely possible (less than 5 per cent of cases, according to Schmieden and Sebening) and even allowing for the likelihood that such a small concretion often escapes into the duodenum after determining the necrosis and thus fails to be observed, it is clear that only a minority of cases can be explained on such a basis. In this connection, however, it may be noted that pancreatic necrosis has been found associated with obstruction of the papilla by lesions other than stones, *e.g.* a round worm.

Archibald suggested, as an explanation of cases in which no stone is found, that a similar obstruction, permitting reflux of bile along the pancreatic duct, might be produced by spasm of the sphincter of Oddi such as might arise reflexly in the same way as pylorospasm in the course of cholecystitis. In support of this view he showed that in cats contraction of the sphincter of Oddi will withstand a pressure of 35 cm  $H_2O$ , and that under these conditions infected bile introduced under pressure into the gall bladder is forced up the pancreatic duct and regularly gives rise to pancreatic necrosis.

It is well known that the anatomical relationship of the bile and pancreatic ducts in man is not always of such a character as to permit bile reflux, and many observations have been made to determine the relative frequency of different types of ductal arrangement. The findings of different observers have been highly inconstant. Thus, Opie in 100 routine autopsy cases found an ampullary arrangement such as would allow the two duct systems to become confluent in 89, whereas Mann and Giordano placed the incidence at 3.5%—a low estimate which may perhaps be explained by the fact that they used formalin hardened specimens without proper allowance for shrinkage of the ampullary tissues. Probably a more reliable estimate is that given by Cameron and Noble, who prepared casts of the ducts by injecting fusible metal after obstructing the papilla by means of a small stone, under these conditions the bile and pancreatic ducts were found to communicate in 75% of cases.

These anatomical variations in routine autopsies have, however, little bearing on the matter, far more important is the arrangement of the ducts in cases of pancreatic necrosis. Unfortunately, there have been very few observations on this subject, owing, no doubt, to the fact that in these cases the gland is friable and the ducts can be found with difficulty. Isolated cases have been reported, however, in which the ducts opened separately into the duodenum, and rare cases have also been described of necrosis confined to the area drained by the accessory

duct of Santorini To explain such cases it has been suggested that the activation of trypsinogen might have been caused by reflux of intestinal contents from the duodenum, but it must be admitted that such an explanation lacks conviction

Whilst the evidence cited above points clearly to a reflux of bile as the main aetiological factor in many cases of pancreatic necrosis, it cannot be regarded as a sufficient explanation in all Apart from the direct evidence provided by the isolated examples already mentioned, in which the ducts have been shown to open separately into the duodenum, there are many cases in which the occurrence of biliary reflux would seem to have been improbable Rich and Duff have drawn attention to a *proliferative metaplasia* of the duct epithelium similar to that seen in the breast in chronic mastitis, and have suggested that the obstruction of the pancreatic duct caused in this way may be responsible for the escape of trypsinogen into the interstitial tissues of the gland On the other hand, the frequent association of pancreatic necrosis with chronic cholecystitis lends support to the old view, first put forward by Margaret, that a lymph borne infection may sometimes be responsible for initiating the auto-digestion, whilst, finally, the occasional occurrence of pancreatic necrosis in the course of typhoid fever, mumps and other diseases suggests that in some cases a blood-borne infection may be an aetiological factor

### CHRONIC PANCREATITIS

Minor degrees of induration of the pancreas are found not infrequently at operation for gall stones, especially when a stone has been impacted in the common duct In some such cases the presence of scattered points of necrosis or calcification points to an earlier mild attack of acute pancreatitis

The term *Chronic Relapsing Pancreatitis* has been applied to a condition occurring mainly in men, and unrelated to biliary disease, in which the pancreas is diffusely hard or nodular and microscopically shows fibrosis with cellular infiltration Sometimes there has been a history of recurring attacks with severe pain Eventually progressive destruction of the gland may lead to diabetes and steatorrhœa, while there may be calcification or a calculus may form in the pancreatic duct

Constriction of the common duct by fibrosis may give rise to jaundice and cause confusion with carcinoma, especially if there has been little or no pain This may account for some cases of unexpectedly long survival in supposed cases of carcinoma

### PANCREATIC CYSTS

Pancreatic cysts are rare Their surgical importance lies in the fact that they must be taken into consideration in the differentiation of other cystic tumours in the abdomen

It is customary to divide cysts of the pancreas into *true* and *false*, according as they arise in the gland itself or merely in proximity to it.



### True Pancreatic Cysts

True pancreatic cysts are much rarer than false ones. They may originate in many different ways and the following varieties may be recognized (1) Retention cysts (2) Degeneration cysts (3) Congenital cystic disease (4) Dermoid cysts (5) Hydatid cysts (6) Hæmorrhagic cysts

(1) **Retention Cysts.** Cystic dilatation of the ducts of the pancreas may result from obstruction by calculi, from fibrous stenosis of the main duct, and from chronic pancreatitis. The dilatation may be widely distributed but is rarely very great.

(2) **Degeneration Cysts** may arise either in an adenoma or in a carcinoma. The cyst is usually multilocular and is situated in the head of the pancreas. It contains clear or mucoid fluid, which may be blood stained.

Multiple cysts are present very frequently in association with angiomatic tumours of the cerebellum and spinal cord—Lindau's disease. Cysts or a hypernephroma may coexist in the kidneys.

(3) **Congenital cystic disease** is exceedingly rare, it has been found usually in children. The condition resembles that met with in the kidneys, with which it may coexist. The lungs, too, may be the seat of cystic disease which is liable to fatal suppuration in early life.

(4) and (5) **Dermoid and Hydatid cysts** have been found in the pancreas. They possess no special features other than those peculiar to the site in which they arise.

(6) **Hæmorrhagic Cysts.** Bleeding may occur into the pancreas as a result of injury or from acute inflammation, and from either of these causes a cyst may develop, but blood may be found in almost any variety of pancreatic cyst.

### False Pancreatic Cysts or Pseudocysts

A pseudocyst differs from a true cyst of the pancreas in that it does not originate in the substance of the gland but is situated in close proximity to it and is generally connected with it. At operation it may be difficult to determine the exact relationship of the cyst to the gland or, indeed, to be certain whether it is a true or false cyst. A true and a false cyst may coexist.

**Ætiology.** A pseudocyst is due usually to the encapsulation of extravasated fluid in the peripancreatic cellular tissues or in the omental bursa. Its mode of origin is not always clear as a satisfactory history cannot always be obtained. Many cases are due to injury, and follow a blow on the epigastrium which causes laceration of the posterior layer of the small peritoneal sac and of the pancreas. Blood and pancreatic secretions are poured into the omental bursa or into the cellular tissues around the pancreas, the epiploic foramen becomes sealed, and the peritoneum becomes condensed around the effusion and brings about its encapsulation. The resulting swelling in the upper part of the abdominal cavity may be evident within a few days or a few weeks of injury, or it may not be detected for many months. In some cases the origin of a pancreatic cyst may be traced to a mild attack of pancreatitis,

which causes an outpouring of blood and pancreatic ferments into the tissues around the pancreas

**Pathological Features** A false pancreatic cyst varies in size from an orange to larger than a fetal head. The thickness of the cyst wall varies, but usually it is quite thin, its lining is generally smooth, although ridges and septa are sometimes present. Old blood clot may adhere in places to the wall of the cyst. Some cysts are multilocular. The lining of the cyst is sometimes composed of cylindrical epithelium, but in many it is fibrous. The contents of the cyst may be clear and watery or gelatinous but more often are light brown from extravasated blood. In a few instances the fluid may have a green tinge from the presence of bile. The fluid contains albumen, is alkaline in reaction and of low specific gravity and on analysis is found to contain very little solid matter. The most important character of the fluid is its *lack of digestion*. All three pancreatic ferments may be present, but often there is only one. In some, especially old encapsuled cysts, no ferments are found or the ferments may be present in an inactivated form. The presence of all three ferments points to a cyst arising from or directly connected with the pancreas, but their absence does not exclude a pancreatic origin. The finding of a starch-converting ferment alone is of little value in diagnosis because it has been shown that fluid from other abdominal cysts or even ascitic fluid may possess such properties. It is a familiar observation that when a pancreatic cyst is drained excretion of the skin and digestion of the subcutaneous tissues may occur from the leakage of the enzyme-containing fluid.

A pancreatic cyst may arise in or be related to any part of the gland, but most frequently it is in the neighbourhood of the body or the tail. In the majority the cyst lies behind the posterior layer of the peritoneum forming the omental bursa. The ultimate position and relations of the cyst are determined by its relations to the peritoneal reflections which form the omental bursa. Thus a cyst may protrude between the stomach and liver or (and this is most frequent) between the stomach and transverse colon. Occasionally it has entered the layers of the transverse mesocolon, and the colon is stretched over its surface. A cyst in the head may cause pressure on the common bile duct and pancreas. The many variations in position lead to great difficulty in differential diagnosis, and to confusion with other abdominal cysts—for example, a dilated gall bladder, a cyst of the common bile duct, a cyst of the posterior wall of the stomach, a collection of ascitic fluid and hydronephrosis. Spontaneous rupture is a rare occurrence.

In the treatment of a pancreatic cyst, marsupialization of the cyst wall and drainage are usually sufficient. Complete removal of a large cyst, unless it is pedunculated, may be attended by great risk on account of the large and often dilated vessels that surround it and because of its firm adhesion to neighbouring structures.

### PANCREATIC CALCULI

Calculi in the pancreatic ducts are rare. Men are affected more often than women (4:1).

Calculi are never found in a healthy pancreas, and it seems probable that they are the result of catarrh of the ducts from infection. The number of calculi varies, usually five to ten are present, in rare cases there is a solitary calculus, but as many as 300 have been found. The calculi vary in size from fine gritty material to masses the size of a date stone or a walnut. They may be smooth or rough, soft or hard, and in colour white, grey or yellow.

A pancreatic calculus is chiefly composed of phosphate and carbonate of calcium, but examples containing oxalates are described. On account of their content of lime salts they cast a shadow in a radiogram, and this is helpful in their recognition.

The calculi may be found in all parts of the ducts of the pancreas, but the head is the usual site.

A pancreatic calculus may give rise to symptoms which closely resemble biliary colic. In many of the recorded cases gall stones have been present, sometimes with jaundice, and this has diverted attention from the pancreas. In some the presence of glycosuria, azotorrhœa and steatorrhœa may aid in diagnosis by directing particular attention to the pancreas. Sometimes a calculus has been responsible for an abscess.

In diagnosis the presence of a shadow in the region of the pancreas may be helpful. A single calculus in the head usually lies transversely. If the calculi are more numerous and distributed throughout the pancreas diagnosis may be made with considerable certainty.

## TUMOURS OF THE PANCREAS

### Simple Tumours

Simple tumours of the pancreas are rare but as they are usually encapsuled they are amenable to surgical removal. The commonest is an adenoma, which is often cystic (*cystadenoma*). It originates probably in the duct epithelium, and has been found most often in relation to the head of the gland.

**Islet-cell Tumour (*Nesidioblastoma*)** A simple adenoma may arise in the islet tissue of the pancreas. It may possess exaggerated functional activity and give rise to characteristic metabolic features which are known as *hyperinsulinism*. The disease is commonest in middle aged adults especially women.

The adenoma is usually greyish white or pink and ovoid, and may be 2-9 cm in its long axis. It is most common in the body or tail on the superficial surface, but it may be deeply seated in any part of the gland. The tumour has usually a thin capsule but in some instances local infiltration has been observed, but definite malignancy with metastasis is very rare. Microscopically, an islet cell adenoma is composed chiefly of branching solid trabeculae two or more cells thick, and separated by strands of fibrous tissue rich in blood vessels. The cells are mostly basophilic and resemble the normal  $\beta$  cells of the islets and are polyhedral or columnar with abundant granular cytoplasm containing a round or oval nucleus which stains deeply with hæmatoxylin.

An islet cell tumour may give rise to periodic attacks like those due to an overdose of insulin and characterized by dizziness, somnolence, etc. The attacks may be precipitated by prolonged fasting and when they occur may be relieved by giving large quantities of glucose. The blood sugar is constantly low, varying between 0.02% and 0.05%.

In cases of suspected hyperinsulinism, provided other causes of hypoglycæmia can be excluded, surgical exploration is warranted, and in the cases in which the tumour has been removed and the patient survived there has been complete recovery. At operation discovery of the tumour may be difficult, or, if it is deeply embedded, impossible. There may be more than one tumour. In some cases there is no tumour but generalized overgrowth of the islet tissue.

### Malignant Tumours

The pancreas especially its head, is very frequently involved by the extension of a carcinoma of the stomach, and such a growth is more

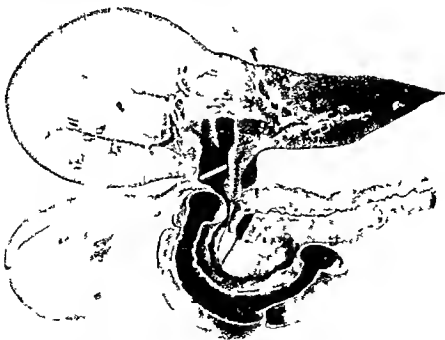


FIG. 26a. Carcinoma in the head of the pancreas. The tumour is small and has occluded both the pancreatic and the common bile duct. There is a very marked dilatation of the common bile duct and the intrahepatic ducts. The gall bladder is moderately dilated.

common than a primary malignant tumour. Metastatic tumours from the lung, breast, etc., are common.

**Types of Growth.** A primary carcinoma may begin in the glandular epithelium or in the cells lining the excretory ducts, and the microscopic structure is determined by this difference in origin. A cancer arising

from the glandular epithelium is of a spheroidal cell pattern, it is much more common and is of more rapid growth than the columnar cell type derived from the ducts. The spheroidal cell tumours are usually of a scirrhus type, although a bulky encephaloid tumour is sometimes observed. In all varieties mucoid, cystic or hæmorrhagic changes may occur. Calculi have been discovered in the interior of some tumours, and have been held responsible for their development.

Malignant tumours seldom attain a very large size. The growth is usually hard, irregular, and nodular on its surface, and it is securely fixed to neighbouring structures. The cut surface of the tumour is usually of whitish grey or yellow colour, and degenerative changes are often noted in it. In about 56% of cases the tumour is in the head of the pancreas, the body is the next most common site (6%) and the tail is but rarely involved. In a considerable proportion (30%) the whole gland is involved diffusely by a multinodular type of growth that causes a generalized and fairly uniform enlargement of the pancreas.

**Pathological Effects.** The pathological effects vary according to the situation and the direction of extension of the tumour. When, as is most common, the growth is in the head it causes compression of the pancreatic duct and may obliterate it completely so that at autopsy the whole duct system proximally may be widely dilated. The common bile duct is usually subjected to pressure or compression at an early stage although its involvement may be long delayed or may never occur. Obstruction of the common bile duct leads to a dilatation of the upper part of the duct and gradually increasing distension of the gall bladder, and in the later stages the intrahepatic ducts are considerably dilated. It is unusual for the tumour to cause much obstruction of the duodenum. Emptying of the stomach may be interfered with from involvement of the pylorus.

A tumour in the head of the pancreas as it extends may occlude the portal vein or its tributaries or even the vena cava and ascites is the final result. Portal thrombosis has occurred in a few instances. The ureter, colon or stomach may be invaded in the late stages.

Secondary deposits occur with greatest frequency in the liver, either as multiple opaque foci or, more rarely, as a single large mass. The retroperitoneal lymph glands are often involved and through that channel the mediastinal glands may be invaded. In advanced cases metastases of considerable size may occur in the lungs; a single one may simulate a primary tumour.

**The Clinico-pathological Features** are governed by the position of the tumour. The gradual onset of jaundice with obvious enlargement of the liver and the gall bladder is the most striking effect. If the growth starts near the duct jaundice occurs early; otherwise it may be long delayed. Signs of pancreatic dysfunction are rare for anastomoses between the main and accessory pancreatic ducts ensure egress to the external secretion while the internal secretion insulin remains normal since only comparatively few islets are implicated.

In peri ampullary growths arising from the ampulla itself the adjoining pancreas or the duodenal papilla superficial necrosis of the growth may relieve the biliary obstruction and cause the jaundice to be intermittent while infection from the growth may lead to cholangitis thus mimicking the state often produced by a stone in the duct.

A tumour in the body of the gland usually causes pain and a gradual failure of appetite and strength features which make differentiation from carcinoma of the stomach difficult

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## CHAPTER XXX

### DISEASES OF THE SPLEEN

THE surgery of the spleen, once based upon empiricism is now founded on scientific pathological and hematological precepts

**Structure** The structure of the spleen appears very confusing to those unacquainted with its architecture, but actually it is not unduly complicated. The thick fibro muscular capsule and trabeculae enclose a network of branching cells which form the framework of the pulp, and scattered through the pulp lie the Malpighian bodies, which consist of localized thickenings of lymphoid tissue arranged like mantles around the smaller arteries. The structure may best be understood by considering the course of the blood stream. The arteries, after giving off small side branches which terminate in the Malpighian bodies branch in a dichotomous manner, and end in minute penicillar vessels little larger than capillaries, which are surrounded by aggregations of pulp cells known as ellipsoids. From there the blood passes into a meshwork of wide tortuous channels, the sinusoids of the pulp, which have no complete endothelial lining and are essentially clefts between the branching reticulate pulp cells. The sinusoids are of large size compared with the penicillar vessels, and the blood therefore pursues a sluggish course, in places even stagnating for relatively long periods, the blood is thus brought into intimate contact with the pulp cells, and is readily subjected to their beneficent influences. Finally, the blood leaving the pulp spaces is collected into large venous sinuses and thence to the tributaries of the splenic vein.

**Functions** The spleen is not a separate and independent viscus working in isolation and having specific properties, but rather as an organ intimately connected with at least three important systems. It is the most important member of the reticulo endothelial system it takes part in the formation of the blood, especially in the embryo and it is intimately concerned with the metabolism of blood pigment. Consequently, it shares in a special degree the same changes as other organs concerned with hematopoiesis.

The functions of the spleen, so far as they are known or suspected may be classified as follows —

(1) *Hæmatopoietic Function* In adult life this is practically confined to the production of lymphocytes in the Malpighian bodies. Occasionally in disease the spleen may resume its embryonic property of producing red cells and polymorph leucocytes.

(2) *Hæmatoclastic Function* As the most important member of the reticulo endothelial system the spleen ~~and that it therefore~~ adequately recovers with the destruction of blood cells in the meshes of the pulp and are here seen

Their haemo globin content is set free and becomes converted into intermediate products which are either stored or despatched to the liver for excretion in the bile. Probably the spleen also destroys blood platelets, for it is found that in diseases characterized by a great diminution in platelets removal of the spleen is followed by their reappearance in normal numbers.

(3) *Phagocytosis of Particulate Matter* In its sluggish flow through the sinusoids the blood comes into intimate contact with the phagocytic cells of the pulp and these exercise the most important action of removing organisms and other foreign or noxious particles present in the circulating fluids. This phagocytic action may be demonstrated readily in the animal by injecting some particulate substance such as Indian ink into the blood stream, when the spleen rapidly becomes loaded with pigment and assumes a deep black hue. This may be of importance as a protective mechanism in infective diseases and in the occasional minor disturbances of everyday life.

(4) *Reservoir Function* The capsule and trabeculae contain plain muscle fibres embedded in the connective tissue, and in virtue of these the spleen is an actively contractile organ which, in response to certain stimuli, undergoes reduction in size to a very considerable extent. The importance of this property lies in the fact that in health when the body is at rest the spleen contains a large fraction of the total blood volume—occasionally, it is claimed as much as one-fifth—and when under certain conditions the need for this blood arises the spleen is able to expel it into the portal circulation.

These variations in size serve to regulate the degree of congestion of the liver and the alimentary canal during the phases of digestion, and also enable the spleen to respond to the demand for sudden increase in the red cell content of the circulating blood, for example, during exercise and in asphyxia, carbon monoxide poisoning and haemorrhage.

(5) *Effect on Fragility of Red Cells* Red cells expressed from the splenic pulp are more fragile than those circulating in the blood stream, as estimated by their readiness when placed in graduated hypotonic salt solutions. Moreover, in conditions characterized by excessive fragility of the circulating red blood cells it is found that removal of the spleen is generally followed by a return of the cells, almost, or entirely, to their normal state. These observations have suggested that the spleen normally, and in certain diseases to a greater degree, increases the fragility of the red cells.

(6) *Production of Antibodies* In certain animals it is found that splenectomy is followed by a diminished resistance to infections, and it has been thought that the spleen may be an important site for the production of antibodies. Confirmation, however is lacking.

*Effects of Splenectomy* Removal of the spleen is followed by temporary leucocytosis and temporary anaemia of the secondary type. The

leucocytes fall off in a few weeks but occasionally

When the blood platelets have been destroyed there is a rapid return to the normal, but when the number before operation



has been normal there is usually little change, though sometimes an increase even to fivefold has been noted, and this probably predisposes to thrombosis. The fragility of the red cells is decreased in the healthy animal after splenectomy, and the same sometimes is observed in man, particularly if increased fragility has been present before operation.

One of the most valuable effects of splenectomy is a purely mechanical one, namely, that of eliminating the splenic blood flow and thus diminishing the quantity of blood reaching the liver. It is said that in health the spleen transmits a quarter of the portal blood, and when the spleen is large and very vascular, as in splenic anæmia, the proportion transmitted must be much greater. To a liver embarrassed by cirrhotic change the reduction of the portal circulation must bring great relief.

**The Rationale of Splenectomy.** Except in injuries or in undue mobility of the spleen, splenectomy should only be advised upon some definite indication based upon pathological considerations. The days of splenectomy for mere splenomegaly are past, and in practice there are three major indications for the operation —

- (1) To remove a focus of disease, e.g., a tumour or cyst
- (2) To reduce the volume of blood in the portal circulation
- (3) When there is evidence that the spleen is engaged in excessive destruction of, or damage to, the cells of the blood

The last indication is of especial importance in atypical disorders of the spleen and blood-forming tissues. In progressive anæmia of unknown origin with a large spleen it is essential to decide whether the spleen is primarily involved and is the cause of the anæmia, or whether the splenic enlargement is compensatory. In such a case much can be learnt from two procedures, namely, estimation of the fragility of the blood cells and enumeration of the reticulocytes.

*The fragility of the red cells* is measured by their resistance to hypotonic saline solutions. Normal blood added to a graduated series of saline solutions lyses when the concentration of sodium chloride is reduced to about 0.35% or 0.4%, but fragile cells lyse more readily, at 0.5% or 0.6%.

*The reticulocyte count* is even more valuable. A reticulocyte is merely an immature red cell, and it differs from the adult cell in possessing a delicate reticulum, which is invisible in films stained by the usual methods, but can be demonstrated readily by the use of vital stains. It is probable that all red cells are at first reticulate, but in health reticulocytes are present in only very small numbers in the circulating blood. An increased count indicates an exaggerated erythroblastic activity of the bone marrow.

In aplastic anæmia or where the bone marrow is diseased and unable to proliferate, no reticulocytes are formed, whereas in acholuric jaundice, when the bone marrow is attempting to replace the cells destroyed in the spleen, the count may rise even to 85%. In progressive anæmia a high reticulocyte count indicates that if the hæmolytic agent be removed, the bone marrow will adequately recover its normal activity.

## INJURIES OF THE SPLEEN

The spleen may be pierced in stab wounds, or rarely by a sharp fragment of a broken rib forced through the diaphragm. A much more common injury, however, is rupture resulting from indirect violence. Rupture of the spleen generally occurs as a result of a severe crushing or "run over" injury, and it may be accompanied by others, such as fractured ribs, rupture of the liver, a tear of the diaphragm or fracture of the spine. An enlarged spleen, especially one which is soft and friable from disease, may be ruptured by a comparatively slight injury or even spontaneously—perhaps as a result of a sudden contraction of the plain muscle fibres in its capsule. Cases have been described of spontaneous rupture of a normal spleen.

Rupture generally involves the vascular pedicle and leads to hæmorrhage into the peritoneal cavity. At first the bleeding is slow, owing to the degree of shock, and a hæmatoma forms in the left upper quadrant of the abdomen, but after a few hours, when the blood pressure rises, bleeding becomes more profuse. In rare cases severe hæmorrhage may be delayed a day or two, or even a week.

## EXCESSIVE MOBILITY OF THE SPLEEN

A spleen enlarged from any cause, and occasionally a spleen of normal size, may stretch its retaining ligaments and attain considerable mobility, so that it swings freely to any part of the peritoneal cavity. Such a spleen may cause discomfort on account of its weight and mobility, and, moreover, it is apt to give rise to symptoms from torsion of its pedicle. Such a mobile spleen may rarely give rise to secondary effects from pressure. Cases have even been recorded in which the spleen became impacted in the pelvis, and pressed upon the bladder and rectum.

## CYSTS OF THE SPLEEN

Cysts of the spleen are rare, and their origin is obscure. The majority are spurious cysts, the result of hæmorrhage or of degenerative changes from infectious or vascular disease. Hydatid cysts and dermoid cysts have been described from time to time.

Primary non-parasitic cysts may be classified as single or multiple. Single cysts, which are rare, have been observed generally in young adults. They may attain considerable size and may fill the greater part of the abdomen, so as to be mistaken for an ovarian cyst. Such cysts contain serous fluid often loaded with cholesterol crystals. The cyst may have an endothelial, epidermoid or a fibrous lining, or a combination of all. Calcification in the walls is sometimes present.

Multiple cysts of the spleen sometimes occur in association with polycystic disease of the kidneys and liver.

## TUMOURS OF THE SPLEEN

Primary tumours in the spleen are extremely rare. Carcinoma, sarcoma, and angioma have been described. Of secondary tumours,

those arising in hæmatopoietic tissues, *e g*, multiple myeloma, are the most common. Occasionally the spleen is involved in tumours growing from neighbouring organs, such as the stomach or the left kidney.

The rarity of tumours of the spleen presents a problem of great interest in relation to the general features of cancer growth, for although the spleen has lymph vessels only about its capsule, its blood supply is copious, and one would expect it to afford a favourable site for proliferation of cancer emboli. There is no doubt that many cancer cells reach the spleen, but fail to establish themselves, and it would seem that the spleen possesses a not yet understood property of inhibiting their growth. In this respect it resembles muscle which too is another rare site of secondary tumours.

### OTHER SURGICAL DISEASES OF THE SPLEEN

There remain for consideration certain affections of doubtful nature, which are characterized by a variable degree of enlargement of the spleen and by many more widespread changes. Certain of these may be regarded as primary diseases, others are diseases in which the spleen merely participates. The classification of these diseases presents many difficulties owing to the diversity of their manifestations, which, moreover, differ in detail in almost every individual case, and their ætiology constitutes one of the most difficult problems of hæmatology. For simplicity, however, it will suffice here to describe only those of surgical interest, *viz* (1) acholuric jaundice with erythrocytic fragility, (2) splenic anæmia, (3) thrombocytopenic purpura.

A fourth condition, the distinct entity known as Egyptian splenomegaly, is outside the scope of this book, and it will be sufficient to state that it results from schistosomiasis (*bilharziasis*), and that in its pathology and effects it closely resembles splenic anæmia.

### ACHOLURIC OR HÆMOLYTIC JAUNDICE WITH FRAGILITY OF RED CELLS

There are many types of hæmolytic jaundice, but the only one of surgical interest is that associated with fragility of the erythrocytes. This is usually congenital, and then often familial, but it may be an acquired affection. It is characterized by mild jaundice, variable in degree but persistent throughout life, secondary anæmia and moderate enlargement of the spleen.

The essential feature of the disease is an increase in the fragility of the red blood cells. When blood is added to hypotonic salt solutions of gradually diminishing strength, a stage is reached at which lysis or laking of the red cells begins. In health, this point is reached when the concentration of sodium chloride is reduced to 0.35% or 0.4% whereas in conditions of undue fragility it is reached earlier at perhaps 0.5% or 0.6%. The effect of this fragility is to cause an excessive breaking down of the abnormal cells by the spleen, with consequent liberation of excessive amounts of blood pigment. There is an excess of a pigment closely related to bilirubin in the blood, and the bile is heavily laden with

pigment. The faeces remain coloured, and, as the bilirubinæmia is of mild degree, there is no overflow of bile pigments into the urine. To compensate for this hæmolytic the bone marrow rapidly discharges young red cells into the circulation and consequently the reticulocyte count may be increased even to 85% (*see p 594*). Many of the red cells are spheroidal (spherocytes).

Where the disease is congenital, the symptoms are usually mild, and slight jaundice with anæmia is the only manifestation. In some cases, however, and more commonly in the acquired form of the disease the anæmia is more severe and there may be occasional exacerbations of the jaundice with pain in the upper abdomen and fever, which may simulate cholelithiasis. In many cases gall stones are formed as the result of the disturbance of pigment metabolism. The stones are of the "pure pigment" type (*see p 538*).

The spleen is invariably enlarged in acholic jaundice, usually only to a moderate degree, occasionally to ten times its former bulk. Adhesions are rarely present. Microscopically, the only gross change usually found is a marked increase in the vascularity of the pulp, but if the spleen has been removed during an active phase of the disease there may be an excess of blood pigment.

Recent work indicates that the congenital and acquired forms differ in ætiology. In the congenital type red cells transfused from the patient into a normal person survive only a short time while cells transfused from a normal donor into the patient survive normally. Thus in this type hæmatopoiesis is abnormal i.e. the cells as formed in the marrow are abnormally sensitive to the normal hæmolytic mechanism.

In the acquired type the reverse holds good. The patient's red cells when transfused into a normal host survive normally, whereas healthy cells transfused into the patient are destroyed rapidly. Thus in this type hæmatopoiesis is normal and the red cell destruction is due to the presence of abnormal hæmolytic agents.

### SPLENIC ANÆMIA (Banti's Disease)

The syndrome described by Banti in 1894 is characterized by splenomegaly and anæmia often complicated by hæmatemesis and followed by cirrhosis of the liver with ascites. Formerly it was believed that the primary focus of the disease lay in the spleen and that cirrhosis of the liver if it supervened was a secondary feature, due perhaps to the action of toxins elaborated in the spleen.

Recent work, however, indicates that the splenic enlargement is simply the result of long standing elevation of the portal blood pressure—portal hypertension. Commonly the hypertension is due to obliteration of the venous channels within the liver, as a result of pathological changes which subsequently become manifest as hepatic cirrhosis. Less often it is due to congenital atresia or malformation of the portal vein, to pressure on the portal vein by tumour, cyst or gumma, or to thrombosis of portal or hepatic or splenic vein occurring primarily or as a result of such lesions as trauma, pancreatitis, etc.

In health the pressure within the principal veins of the portal system ranges from 5 to 10 c cm of water. In portal hypertension it may rise to 30 or even 50 c cm. This rise of pressure is responsible for the dilated and tortuous character of the splenic vein and its tributaries which is a well recognized finding at operation.

The changes in the spleen are also due directly to the venous hypertension. The spleen is considerably enlarged of grey pink colour and firm consistency. Microscopically the most characteristic feature is the presence of *siderotic nodules*—particles of iron pigment embedded in fibrous tissue—which are situated mainly round the central arterioles of the Melpighian corpuscles. Such nodules are believed to be due to minute peri arterial hæmorrhages resulting from the venous congestion.

The portal hypertension leads to the development of collateral channels between the portal and systemic venous systems notably at the œsophagus (between the gastric veins and œsophageal veins draining to the azygos vein) at the umbilicus (between vessels in the falciform ligament and abdominal wall) and at the anus (between superior and inferior hæmorrhoidal vessels). New channels also develop at the upper pole of the spleen where the enlarging viscus by stretching its lienorenal ligament has become "adherent" to the diaphragm, and in the retroperitoneal tissues in relation to the pancreas, duodenum and colon. Of these many sites of collateral dilatation, the œsophageal holds primary classical importance, for the great varices which form under the mucous membrane commonly lead to hæmorrhage which may prove fatal.

The blood changes in splenic anæmia are characterized by anæmia and neutropenia. The red cells may be reduced to 3 000 000 per c mm and are small, poikilocytic and hypochromic. The total white count may be reduced to 3 000 per c mm. The platelets may also be reduced in number. In part the anæmia is commonly due to hæmorrhage but it may occur with no overt evidence of hæmorrhage, and its character, coupled with the observation that the lymphocytes are usually unaffected, suggests that the release of cellular elements from the bone marrow is inhibited perhaps as a consequence of the splenic disorder.

Understanding of the pathology of the Banti syndrome as of all other diseases is of profound importance in regard to surgical treatment. Splenectomy, though partially effective by virtue of reducing the flow of blood into the portal field is only completely curative in those rare cases where the venous obliteration is limited to the splenic vein while in other cases it carries the disadvantage of eliminating the collateral channels to the diaphragm. The old treatment by omentopexy was well conceived, but its effect negligible. The modern operation of porto caval anastomosis effectively by-passes the obstruction and averts its most dangerous manifestation, œsophageal hæmorrhage. Arterial blood *via* the hepatic artery suffices to maintain the nutrition and oxygenation of the liver, while the diversion of portal blood causes little impairment—as the physiologist Eck showed as long ago as 1877—in the manifold processes of metabolism and detoxication for which the liver is responsible.

## THROMBOCYTOPENIC PURPURA (Essential Thrombopenia)

There are many forms of purpura, that is, of diseases characterized by a tendency to hæmorrhagic extravasations. In some, the changes in the blood are obviously secondary, as in the case of the so-called symptomatic purpura of septicæmia, miliary tuberculosis, etc.; in others, the blood changes appear to be primary.

The only variety of surgical interest is one of the primary group which is known as thrombocytopenic purpura. This is a disease manifesting itself intermittently in otherwise healthy persons, usually adolescents, and characterized by cutaneous hæmorrhages, slight recurring fever, and splenomegaly. The blood changes during the attacks are characteristic. The essential feature is a decrease in the number of platelets (thrombocytes) almost to zero, and this results in marked increase in the bleeding time as estimated by the duration of flow of blood from a small puncture of the lobule of the ear. From the normal range of 2 to 4 minutes this may be increased to 15 minutes or longer. It is a remarkable fact that although bleeding from the capillaries is so prolonged, blood withdrawn and tested for coagulation *in vitro* clots in the normal period. A further factor in prolonging the bleeding is found in the failure of the blood clot to retract.

Hæmatologists are not yet agreed as to the mode of origin and of destruction of the blood platelets, or even that they exist as cellular entities, and consequently there is no definite knowledge of the cause of thrombocytopenia. One view is that the actual production of platelets is unaffected but that the normal platelets are destroyed in excessive numbers by the spleen.

Another important but little understood feature of the disease is an increased permeability of the capillary walls, which are liable to rupture with undue ease. This may be clearly demonstrated by the test of Hess and Frank, which consists in applying to the arm a tourniquet or sphygmomanometer band. When the pressure is gradually increased to obstruct the veins, a crop of purpuric spots will rapidly develop, both under and distal to the tourniquet.

It must be remembered that in many of these cases there are only mild recurrent attacks. Splenectomy is indicated in severe cases where there is actual risk to life from hæmorrhage, and is more likely to be successful in chronic than acute cases, in which relapses are not uncommon. After splenectomy the platelet count rapidly increases to normal, the bleeding diminishes and hæmorrhages cease.

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## CHAPTER XXXI

### DISEASES OF THE ADRENAL GLANDS

LIKE the pituitary the adrenal glands are composed of two distinct tissues the medulla ectodermal the cortex mesodermal—with independent functions.

The medulla is intimately related to the autonomic nervous system. It is derived from neuro-ectoderm, and it acts, through the agency of its secretion adrenalin, upon the sympathetic nerve endings. Its tumours are of two types. One variety is composed of adrenalin secreting cells and is known as chromaffin-cell tumour or phæochromocytoma. The other is composed of nerve cells or their progenitors and is known as a neuroblastomata.

The cortex, on the other hand is of mesodermal origin and appears first in the embryo as a ridge close to the mesonephros (Wolffian body). It is composed principally of large cells rich in cholesterol, for which it is probably a storehouse. Its tumours are composed of cells of similar type. The cortex has functions essential to life, whose nature are not clearly understood, and its complete removal or destruction inevitably causes rapid death. It appears to influence secondary sexual characters, and in tumours of the cortex these are sometimes profoundly altered.

In addition the cortex has an influence on the metabolism of sodium and chloride as witnessed in Addison's disease. In this condition exhibition of the synthetic active principle of the cortex, desoxy corticosterone acetate (D O C.A.) parenterally or by its implantation into the tissues, is effective in controlling the constitutional effects.

### TUMOURS OF THE ADRENAL MEDULLA

The cells of the adrenal medulla are derived from the elements of the primitive sympathetic chain, from which they migrate at an early stage of embryonic life. When mature, they assume the faculty of secreting adrenalin, and may be distinguished microscopically by the readiness with which they take on a brown coloration when treated with chromic acid salts, the reason for their designation as phæochromocytes or chromaffin cells.

Tumours of the adrenal medulla are of two types. In the one, the cells retain their affinity for chromates and their property of secreting adrenalin. In the other, they revert to the structure of nerve cells or the progenitors of nerve cells.

(1) Phæochromocytoma. An adenoma is a common tumour of endocrine glands and may be inactive but in many instances it assumes the specific function of the gland in exaggerated form. An adenoma (chromaffin tumour) of the sup-adrenal medulla shares these characteristics. In all but a few instances it is a simple small vascular



tumour like in cellularity to the immature or adult medulla. The cells are polyhedral or granular and may be in acini; the granules are only detectable in fresh tissue by special staining (e.g. potassium bichromate)—they contain adrenalin in excessive amount, a feature which bears evidence of the secretory potential of the tumour.

The factors which govern the secretory activity of the tumour are not understood. The clinical manifestations commonest in women between twenty and forty years are due to excessive release of adrenalin either intermittently or continuous and accordingly there are two main effects—paroxysmal or persistent hypertension—the paroxysmal type in its later phases may assume persistent character.

Subjects of this disorder are unduly susceptible to minor emotional and other stimuli and are therefore specially subject to operation shock.

(2) **Nerve-cell Tumours** These tumours may be highly malignant, and reproduce nerve cells in very immature form (neuroblastoma), or they may be benign and reproduce ganglion nerve cells of adult type (ganglioneuroma). Intermediate types may be recognized.

Neuroblastoma and ganglioneuroma are not limited to the adrenal medulla, but may arise from any part of the autonomic nervous system, for example in the retroperitoneal tissues or in the mediastinum. Tumours similar to a neuroblastoma may originate also in the retina.

**Neuroblastoma** (Sympathicoblastoma) This tumour occurs in infancy or childhood. It is highly malignant, metastasizes early, and often leads to a fatal issue in the course of a few months. The tumour sometimes attains large size, but often is permanently small and may remain unrecognized even at autopsy, or be mistaken for a secondary nodule. It forms a soft fleshy mass, very prone to hæmorrhage and degeneration and it tends to invade surrounding tissues and neighbouring organs—for instance, the liver or spleen. The kidney is not always invaded, even though indented and compressed.

Microscopically, the tumour closely resembles a sarcoma, and for this reason its true nature was not recognized until 1910 (J. H. Wright). It is now clear that the origin is from nerve tissue and it seems probable that most retroperitoneal tumours of infants previously described as round cell sarcoma are of this nature. The cells are small, round or oval, with large hyperchromatic nuclei and scanty protoplasm and sometimes arranged in rosettes. Interspersed between groups of the cells are ill defined fibres, which have been identified by special staining reactions as axis cylinder processes and neuroglial fibrils.

The *metastases* of adrenalin blastoma occur early and are often the first evidence of the disease. Dissemination occurs by direct invasion by lymphatic channels and by the blood stream. There is a remarkable tendency to metastasize in the cranial bones near the orbit, and such growths are very apt to be mistaken for primary tumours. Metastases occur also in the liver, spleen, lungs, ribs, peritoneum and other tissues.

Two clinical types of the disease have been described according to the sites affected by metastases.

Pepper in 1901 described the type associated with his name. The tumour is usually situated in the right adrenal gland, and the characteristic feature is the presence of metastases in the liver, which

becomes greatly enlarged, soft and haemorrhagic, and may fill the greater part of the abdomen completely overshadowing the primary growth. Hutchinsson described a type characterized by the liability to secondary growths in the orbit and neighbouring parts. The metastasis may displace the eyeball and destroy it. The cranial bones affected by the tumour develop feathery projections like the "sun ray" spicules of periosteal sarcoma (*see* Fig 266). The two types are by no means distinct and it should be emphasized that in most cases there are metastases in situations other than the liver and orbit.

**Ganglioneuroma.** This rare tumour is of particular interest on account of its ganglion cell structure which in ordinary circumstances is



FIG. 266. Cephalic metastasis from a neuroblastoma of the adrenal gland. Note the large amount of new bone arranged in spicules perpendicular to the calvaria.

(Museum of Royal College of Surgeons of Edinburgh.)

incapable of division. The tumour may affect adults or children. Intermediate forms of tumour occur having in different parts the characteristics of ganglioneuroma and of neuroblastoma (*see* p. 320). Microscopically there are numerous nerve ganglion cells which lie in groups separated by bundles of medullated and non medullated nerve fibres.

### TUMOURS OF THE ADRENAL CORTEX

Although the adrenal cortex is of mesodermal origin its tumours have a glandular structure and are described as adenoma or carcinoma. In the majority of cases the tumour is an adenoma, a benign encapsulated tumour. Less often though mainly of adenomatous structure, it displays a locally invasive character and attaches itself to the kidneys and perinephric fascia. In some cases, finally, it assumes frankly malignant properties and gives rise to distant metastases.

Whatever the degree of malignancy of the tumour, its naked eye appearances are fairly characteristic. It forms a somewhat globular tumour, yellow in colour, and may attain considerable size. Often it contains cysts filled with clear or bloodstained fluid and hæmorrhages within its substance are common. In general appearance it may closely resemble a 'hypernephroma' of the kidney.

Microscopically, the cells resemble those of the normal adrenal cortex but are arranged atypically. In some cases there is a considerable degree of anaplasia and the tumour may have the appearance of a sarcoma.

The effects of adrenal cortical tumours vary greatly. In approximately 50% the tumour is symptomless or gives rise merely to an aching pain in the loin. In the remainder it causes a remarkable series of effects on the general metabolism and secondary sexual characters—the adrenogenital syndrome. Similar effects also follow functional overactivity of the adrenal gland, and are believed to be due to the elaboration of a hormone or hormones by the cortex.

In general a cortical tumour occurring in an adult is symptomless whereas one in a child or a young woman gives rise to characteristic changes.

*In a male child* the striking feature is virilism. The changes associated with puberty develop early (pubertas præcox). The voice breaks, there is a growth of hair on the face, body and pubic region, the external genitalia of either sex enlarge and the psychological changes characteristic of puberty develop. If the tumour is untreated a brief period of precocious manhood is followed by early senility and death. Sometimes in a male child the most obvious feature is a remarkable muscular development—the infant Hercules type.

*In a female child* the tendency towards virilism is also apparent. Puberty develops precociously, but in most cases there is no menstruation. The skin becomes dry and coarse, the voice is low pitched. The clitoris may be hypertrophied.

*In a young woman* the effects are even more remarkable for they develop rapidly and cause striking changes in external appearance, metabolism and mentality. A girl of pleasing appearance may become within a few months an obese hag.

The victim rapidly becomes obese (gaining as much as 20 to 30 lb in a few months) and assumes a gross plethoric appearance. There is masculine overgrowth of hair and the skin, often the seat of acne, is coarse, dry and scaly.

The internal generative organs—uterus and ovaries—become atrophic. Amenorrhœa is the rule. The clitoris is hypertrophied. The breasts become flattened.

Hypertension is a constant feature—the systolic blood pressure may be raised to 200 mm Hg or higher—and this may cause headaches. Polyuria may occur as a secondary effect.

**Cushing's Syndrome.** The remarkable series of changes described above are not confined to cases of adrenal cortical tumour but occur also in diffuse hyperplasia of the cortex or even in cases in which the cortex appears normal.

Some of these are examples of Cushing's syndrome (*see* p. 290), in which over activity of the adrenal cortex is related to a basophil adenoma of the pituitary gland. Whilst the exact nature of this relationship remains obscure it seems most satisfactory to regard the basophil adenoma as the primary lesion, which in virtue of its hormone stimulates the adrenal cortex to over-activity and thus gives rise to the same effects as a primary growth of the adrenal cortex. Broster and Vines have shown that the potent cells of a cortical tumour contain fuchsinophil granules and that similar fuchsinophil cells are present in increased numbers in the cortex in cases of Cushing's syndrome and in diffuse hyperplasia of the cortex. Thus there is direct evidence of cortical over activity even though on naked eye examination the cortex shows no abnormality. Pecken's work indicates that the adreno-genital syndrome is associated with excessive production of the male hormone androsterone and, by hormone assay, it is now possible to determine whether the pituitary or the adrenal is responsible (*see* p. 290).

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## CHAPTER XXXII

### DISEASES OF THE URINARY ORGANS

**Development of Urinary Tract** In early intra uterine life the urinary tract undergoes a complicated development. Three distinct sets of excretory apparatus appear in turn the pronephros, the mesonephros and the metanephros. The first of these disappears completely after a very brief existence, but the second and third persist in part and in entirety, to form almost the whole of the urinary as well as portions of the generative tracts.

As in lower members of the animal kingdom the primitive excretory organs—the pronephros and the mesonephros—have a segmental distribution. When the embryo becomes segmented in the third week

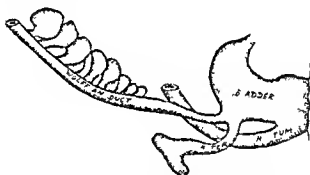


FIG. 267 Diagram showing development of genito-urinary tract  
(After Felix)

of life, each segment receives an excretory apparatus which is placed in a mesodermal mass, the intermediate cell mass, situated on the dorsal aspect of the body cavity. Each excretory apparatus consists of a few minute tubules opening into the body cavity. Those of the cephalad segments constitute the *pronephros*, and they disappear rapidly, leaving no trace, those situated nearer the hind part of the embryo, behind the mid thoracic region, form the *mesonephros* (Wolffian body), and some of them persist. Each Wolffian body, which thus consists of a number of minute tubules embedded in mesoderm projects forward into the coelom or body cavity, and forms a prominent longitudinal ridge lateral to the mid line. At first all the tubules drain directly into the body cavity, but very soon there appears a long excretory channel, which lies in the substance of the Wolffian body, connects its different segments, and extends in a caudad direction as far as the cloaca. This

cases the ureter from the superior renal pelvis enters the bladder at an orifice below and medial to the other

(3) *Faulty Insertion of the Ureter* By some error in the partition of the cloaca the lower end of the ureter may be displaced, and it may open into the prostatic urethra, or into the vagina, or more rarely into the rectum or even the seminal vesicle. The anomaly may give rise to the clinical paradox of incontinent micturition of half the urine combined with normal bladder control of the remainder

(4) *Failure in Ascent of a Kidney* This anomaly is rare apart from fusion, which is described below, but occasionally one kidney may be arrested in the pelvis, or in the iliac fossa, whilst its fellow ascends normally

(5) *Fusion of the Kidneys* In its primitive position at the level of the second sacral vertebra the kidney lies close to the mid line and near its fellow, and the two may readily fuse. The commonest variety is "bilateral fusion" (horseshoe kidney), which is said to occur in approximately 1 of every 800 subjects, but rarely other types of fusion occur. The fused organs may fail to ascend from their pre sacral origin (pelvic kidney) or they may ascend together to one loin (unilateral fusion), and other rare types are described

*Bilateral Fusion (Horseshoe Kidney)* Here the kidneys lie on their respective sides of the mid line, but are connected across the front of the aorta either by an isthmus of renal parenchyma or, more often by a band of fibrous tissue. Usually the inferior extremities of the kidneys are connected, rarely the superior

Anchorage of the kidney to its fellow prevents or perverts the normal process of ascent and rotation. Horseshoe kidneys are usually situated at a low level, with the connecting band in front of the promontory of the sacrum, and often the band is palpable. Since the normal rotation is interfered with, the hilum remains on the anterior aspect of the kidney and the renal pelvis points directly forwards, hence this condition may be recognized in a pyelogram, for the shadow of the renal pelvis is superimposed upon that of the calyces. The kidney is also tilted obliquely or may lie almost transversely, and the ureter, emerging anteriorly, passes down in front of its lower pole. Hydronephrosis is often present, and anomalies of blood supply are common

As in all varieties of renal anomaly, there is an especial liability to infection and calculus formation

A *pelvic kidney* a rare abnormality, lies in the retroperitoneal tissues in the pre sacral region, where it forms a soft mass of irregular shape and variable size, hardly recognizable as renal tissue. Aberrant blood vessels supply it, derived from various neighbouring sources, and there is often some hydronephrosis. The ureters pursue a tortuous course before opening normally into the bladder. From its situation a pelvic kidney is apt to cause obstruction during labour, or it may, even more tragically, be mistaken for a pelvic neoplasm

*Unilateral fusion* is a rare abnormality. One kidney is properly situated in the loin, correctly rotated and with normal ureter and vessels and to its lower pole is attached the other kidney. The displaced

kidney carries across its own ureter, and its own artery, which cross the mid line to their proper side of the bladder and aorta respectively. The translated kidney fails to rotate, so that its hilum and renal pelvis are directed forwards or even laterally

(6) *Other anomalies* of the kidney and ureter include congenital stricture of the ureter congenital hydronephrosis, and polycystic disease. These conditions will be described separately below



### POLYCYSTIC DISEASE OF THE KIDNEYS

This is a disease of developmental origin but it is usually not manifest until early middle life. There is sometimes a definite familial incidence, and Cairns has reported a striking example in which three successive generations of a family were subjects of the disease.

Numerous cysts, small and large, appear in the substance of the kidneys, replacing the renal parenchyma and projecting like bunches of grapes under the capsule. When the condition is fully developed both kidneys are enlarged in greater or less degree, sometimes measuring as much as 25 cm in the long axes. On cross

FIG. 268 Polycystic disease of the kidney. The kidney is greatly enlarged and is replaced by cysts of various sizes. Some of the cysts contained clear watery fluid others a viscid material which clotted on fixation in formalin. The renal pelvis and ureter are of small calibre. The renal arteries are abnormally placed.

(Department of Surgery, University of Edinburgh)

section it is seen that almost the whole renal substance is occupied by the cysts, and the remaining traces of parenchyma are compressed and fibrous. The cysts may project towards the renal pelvis as well as on the surface of the kidney. There is usually little or no dilatation of the pelvis, but sometimes hydronephrosis of the pelvic type exists. More commonly the renal pelvis, though not dilated, is stretched out by the increase in size of the whole kidney, so that the major calyces are elongated and the minor calyces, though of normal shape are far apart.

The contents of the cysts may be thin and watery, or viscid. Sometimes the fluid is clear, of straw colour, containing albumen, urea and

various salts, but not infrequently it is discoloured by old or recent hæmorrhages to various shades of brown and red. The cyst walls are composed of cirrhotic renal tissue and are usually lined by flattened or columnar epithelial cells. The epithelium may proliferate, forming a lining several cells deep or with intracystic projections giving a semblance of a tumour not unlike that in an ovarian cyst.

The theory generally held at present attributes polycystic disease to a failure of union of the active "secreting" tubules and the passive conducting tubules of the kidney. The whole extent of the active tubules, including glomeruli, convolutions and loops of Henle, is derived from the metanephros, and these elements are at first entirely separate from the straight collecting tubules, which grow upwards from the ureter bud (see p. 610). In normal circumstances the two elements unite, but it is thought that incomplete or faulty union may lead to dilatation of the affected tubules.

The features of the disease are of interest in the light of its pathology. Polycystic disease may arise *in utero*, and the foetal kidneys may enlarge so greatly as to obstruct labour, but, apart from this truly congenital variety, the disease rarely becomes manifest until the fourth or fifth decades. During the first thirty or forty years of life there may be no evidence of renal disease, but when at last the disease becomes manifest it often runs a rapid course. The earliest signs may be those of renal failure, anorexia, headache, indefinite gastric disturbances, sometimes the weight of the kidneys causes dragging pain in the abdomen, and their enlargement may attract attention, or there may be sudden hæmaturia. Uremic manifestations lead to a fatal termination. The disease may be complicated in rare cases by infection, by the rupture of one of the cysts or, exceptionally, by tumour formation.

**Other Multiple Cysts in the Kidney.** Small multiple cysts ("retention" cysts) form a constant feature of the granular contracted kidneys of chronic interstitial nephritis, and occasionally one or more of these may grow to large size, and give rise to a palpable swelling in the abdomen. Hydatid cysts may arise in the kidneys, and cysts may occur in relation to new growths in the kidneys.

### SOLITARY CYSTS IN THE KIDNEY

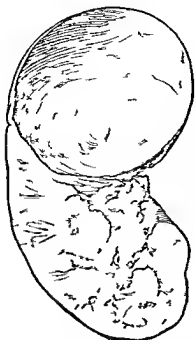
The solitary or "serous" cyst of the kidney is of some rarity, but interesting because it may form a symptomless abdominal swelling whose nature is difficult to define. The condition is one of adult life, the average age incidence being forty five years. The cyst usually projects from the lower pole of the kidney, and it may reach large dimensions. Often it grows with some rapidity and attains the size of an orange in the course of a few months.

With increase in size it gradually becomes pedunculated and it may eventually be freely mobile upon the surface of the kidney. Its wall is composed of fibrous tissue, often thin and translucent and contains clear amber fluid, in which traces of albumen and urea may be found. A lining membrane of flattened or cubical cells may be present, but is



usually incomplete. The cyst does not communicate with the renal pelvis or calyces, and for that reason pyelography may be unhelpful.

The cause of solitary cysts has hitherto been in doubt and they have generally been regarded either as retention cysts from a localized form of chronic nephritis or as congenital lesions comparable to polycystic disease. The experimental work of Hinman and of Hepler, however, has suggested that cyst formation depends upon two essential features (1) obstruction of some of the renal tubules and (2) impairment of the blood supply to a limited area of the renal cortex.



## HYDRONEPHROSIS AND HYDRO-URETER

### *Ætiology*

Hydronephrosis with dilatation of the renal pelvis and calyces is due to obstruction of the outflow of urine. The obstruction may

FIG. 2 Solitary cyst of the kidney  
*Museum of Royal College of Surgeons of  
Edinburgh*

occur in any part of the urinary tract as in the ureter by impaction of a stone or an intra ureteral tumour or by pressure from an extraneous swelling. Obstruction may occur at the ureteral orifice in the bladder from cicatrization or tumour, or in the urethra when the bladder participates in the subsequent changes and the condition is bilateral.

Should the obstruction to the outflow be complete and sudden, as in blockage of the ureter by an impacted calculus kidney function is permanently arrested the ureter proximally and the renal pelvis may remain normal or be attenuated and the hydronephrosis never reaches great size. But when obstruction is discontinuous or only partial as from ureteral stricture prostatic enlargement or urethral stricture, the sequence of pathological events is exactly what takes place in other tubular viscera under similar circumstances viz., utilisation of reserve muscular power with consequent hypertrophy followed by dilatation. In the bladder this is evidenced by thickening of its walls increased trabeculation, and possibly formation of diverticula. In the ureter the walls become thickened, the lumen irregularly distended and the tube elongated and tortuous (hydro-ureter). The hypertrophy is less obvious in the renal pelvis and calyces. The pressure of recurrent accumulation of urine in the minor calyces produces flattening of the renal papillæ, interference with the outflow from the tubules and so back pressure on the glomeruli.

There is coincident interstitial nephritis and the essential structures undergo atrophy, partly from pressure, and partly from interference with the blood supply as the newly formed fibrous tissue in the kidney contracts, but gradually the kidney becomes distended and may reach a very large size, and, then, in its wall renal tissue cannot be recognized by the naked eye, and only in parts on microscopic examination. At any stage of this process, relief of the recurrent obstruction may arrest the progress of the hydronephrosis, but restoration of normal structure and functions in the kidney does not occur.

**Experimental Observations.** Experimental studies have afforded information in regard to the development of hydronephrosis and to the ensuing alterations in urinary secretion. When one ureter is obstructed in rabbits for less than a fortnight the kidney will recover after removal of the obstruction, but if obstruction is maintained for three weeks the kidney atrophies, as its fellow hypertrophies, and there is no stimulus for the obstructed kidney to resume its function after release of the obstruction. If, however, at the time of release of the obstruction the other kidney is removed, the obstructed one responds to the needs of the body and resumes its full function. The conclusion drawn from this finding is that once the secretion of a kidney is seriously impaired the opposite one, provided it is healthy, undergoes hypertrophy and assumes the function of the obstructed kidney—"renal counterbalance." But what seems of greater practical importance is the observation that once hypertrophy has occurred and increased function has been assumed the kidney retains it.

Experiment suggests that increase of pressure in the renal pelvis has a decided influence on the renal circulation, both arterial and venous. First, the veins are obstructed and the kidney is congested, and to compensate for this the arterial pressure rises. Finally, the arteries become compressed and are gradually obliterated. This change occurs first at the cortex and extends progressively to the pelvis. When the blood flow through the glomeruli is slowed down, filtration diminishes and a smaller amount of urine is excreted.

### Varieties of Hydronephrosis and Hydro-ureter

Hydronephrosis and hydro ureter may be congenital or acquired. In many cases there is an obvious cause of obstruction but in some it cannot be demonstrated.

**Congenital Hydronephrosis and Hydro-ureter.** Congenital hydronephrosis may result in enormous dilatation of the kidney, and this may be bilateral, and is then usually incompatible with life. Hydro-nephrosis is sometimes found in association with congenital abnormalities, such as horse shoe kidney, unilateral fused kidney, and double ureter, and in the last example the hydronephrosis is frequently confined to the pelvis and calyces drained by one of the ureters. Congenital abnormalities of the ureter, such as valvular folds of mucous membrane or stenosis of a segment, may be responsible for hydro-nephrosis.

Congenital hydro ureter is rare, it is nearly always bilateral and affects male subjects. It may become manifest in the first few days of

life, because it is noticed the child passes little or no urine; but often the condition produces few effects until later childhood. The hydro-ureter is due to obstruction at the bladder neck in the posterior urethra, either from a disorder of the neuro-muscular mechanism controlling the urethro-vesical sphincter, or to a valvular fold of mucous membrane immediately distal to the orifices of the ejaculatory ducts. The ureters are thin walled, enormously dilated and tortuous (the left usually greater than the right), while the kidneys are hardly affected at all, and in their normal colour and size form a striking contrast to the intestine-like renal pelves and ureters. The bladder is greatly hypertrophied, and as a result of the paralytic state of the ureters reflux of urine occurs by gravitation or by contractions of the bladder. The disease may lead to dwarfism, chronic nephritis and delayed rickets. Death may occur from uræmia or from pyelo-nephritis.

**Hydronephrosis and Hydro-ureter in Pregnancy.** Dilatation of the ureters and to a less extent of the renal pelvis is a normal occurrence in pregnancy. The dilatation usually affects the right ureter alone, and is always less on the left than on the right, possibly owing to the normal deflexion of the uterus to that side. Ureteral dilatation begins about the tenth week and increases progressively as pregnancy advances.

Histological examination of the ureter in pregnancy shows that its muscle and fibrous tissue, especially in the lower portion, undergo hypertrophy similar to that of the tissues of the uterus. When pregnancy is ended the ureter usually returns to normal, but in a few instances dilatation remains.

The cause of the ureteral dilatation in pregnancy has not been fully determined. Pressure may be a contributory factor, but of greater importance is neurogenic obstruction at the lower end of the ureter comparable to achalasia in other organs.

The obstruction at the lower end of the ureter and the resulting stasis of urine probably account for the frequency of *bacillus coli* infection. Apart from infection, the tension within the dilated ureter may be responsible for attacks like renal colic, or, by its effects of increasing the vascular tension in the kidneys, for attacks of hæmaturia.

**Hydronephrosis and Hydro-ureter with Obvious Cause of Obstruction.** Obstructing lesions which may give rise to unilateral hydronephrosis include stones in the kidney or ureter, stricture of the ureter, inflammatory peri ureteritis, and, rarely, tumours of the renal pelvis or of the ureter. Bilateral hydronephrosis may arise from urethral obstruction due to stricture or to prostatic enlargement, from paralytic dilatation of the bladder, from long-continued prolapse of the uterus, or from inflammatory infiltration of the broad ligaments. A calculus in the renal pelvis may cause intermittent obstruction at the pelvi ureteral junction, and this is especially apt to occur when the stone is of small size. Large branched calculi, on the other hand, are not usual in hydronephrosis. Calculi associated with hydronephrosis usually remain small, as their growth is retarded as a result of the diminished amount of crystal forming material in the urine.

Calculi in the ureter may lead to hydronephrosis if the calculus gives rise to sufficient obstruction to raise the tension in the renal pelvis.

The first noticeable change is in the renal pelvis and the calyces, but later the ureter above the stone becomes dilated and may reach the diameter of the thumb. Even minute calculi may give rise to sufficient obstruction to cause hydronephrosis.

**Hydronephrosis and Hydro-ureter without Obvious Cause of Obstruction.** This form of hydronephrosis is usually unilateral. It is very rare in infancy and it is usually found in subjects between twenty and forty years, although it may be much later before it comes under notice. It generally develops insidiously, and it may reach large size without

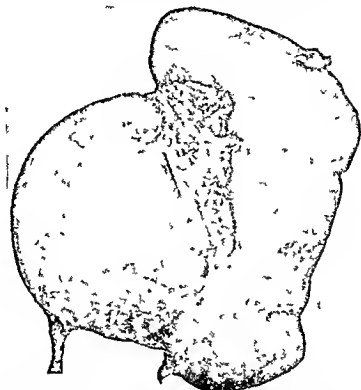


FIG. 270. Hydronephrosis. The renal pelvis is greatly dilated and the kidney is enlarged. On section the calyces were found to be dilated but to a relatively small degree and a considerable amount of secretory tissue remained. The ureter is of small calibre. No cause for the hydronephrosis was found. An abnormally placed artery passed close to the pelvi-ureteral junction to reach the inferior extremity of the kidney.

(Department of Surgery, University of Edinburgh.)

obvious effects. When the kidney is examined at operation no cause for the hydronephrosis can usually be discovered, such cases constitute the majority of examples of hydronephrosis, and receive the non-committal designation *idiopathic hydronephrosis*. It has been suggested that the underlying cause is long continued faulty emptying of the renal pelvis due to inco-ordination of the neuromuscular mechanism of the renal pelvis and the ureter. This explanation lacks full confirmation, but it seems to be the only one which accounts for the obstruction which precedes the dilatation.

Unilateral hydro-ureter—megalo-ureter—with or without hydro

nephrosis, is sometimes present without demonstrable cause. The whole ureter is usually dilated except the intra vesical portion which is normal. The ureter is elongated and thick walled due to overgrowth of the circular muscle coat. The condition is believed to be the counterpart of megacolon and is probably due to disturbance of the sympathetic innervation of the distal end of the ureter resulting in exaggerated tonicity of the uretero vesical sphincter.

**Aberrant Renal Vessels in relation to Hydronephrosis** Pressure caused by abnormal renal vessels has often been blamed for the onset of hydronephrosis. At the hilum of the kidney the renal artery divides into three branches—two superior and one inferior. The inferior branch varies in its point of origin from the main stem, it may leave the parent vessel at any point between the aorta and the hilum of the kidney, or it may even come directly from the aorta. When the inferior vessel is abnormally situated it is in more intimate contact with the renal pelvis or with the ureter, and at its point of contact with these structures there may be fibrous thickening around the vessel. Hydronephrosis is sometimes found in association with such an abnormal vessel, and it is difficult or impossible to say whether the vessel is responsible for obstruction or not. It seems most likely that the vessel is implicated only after the pelvis dilates.

**Abnormal Renal Mobility and Hydronephrosis** Abnormal mobility of the kidney has been suggested as a common cause of hydronephrosis on account of the intermittent ureteral obstruction to which it may give rise. Pyelographic examination has shown however, that hydronephrosis seldom develops even in cases of long standing abnormal renal mobility. Experimentally, Tuffier was unable to produce hydronephrosis in animals by separating the kidney and ureter from their attachments and hydronephrosis did not develop, even when the ureter was looped upon itself.



FIG. 271. Pyelogram of right sided hydronephrosis. The pelvis and all the calyces are greatly dilated. Note the characteristic broadening and clubbing of the calyces.

### Morbid Anatomy

In the early stages of hydronephrosis the capacity of the pelvis of the kidney is increased but the kidney shows little change beyond slight flattening of the renal papillae. The early changes are portrayed in a radiogram after

injection of opaque media, the resulting pyelogram shows dilatation of the renal pelvis, broadening of the major calyces and loss of the 'cupping' of the minor calyces (see Fig. 271).

As the renal pelvis dilates the pelvi ureteral junction may no longer be situated at the lowest part of the pelvis, and a valve like spur may develop between the dependent part of the pelvis and the ureter.

The ultimate form assumed by the hydronephro is depends upon the normal relationship of the renal pelvis to the kidney substance. When most of the renal pelvis is situated outside the kidney (extra renal type) the pelvis, less resistant than the kidney, dilates from increased tension and forms a more or less spherical fibrous sac on which rests the remains of the kidney. The kidney atrophies progressively and may finally be unrecognizable. When the pelvis is mostly enveloped by the kidney (renal type) dilatation occurs within the kidney and the major and minor calyces gradually enlarge at the expense of the kidney substance, which becomes compressed and thinned out over their surface, so that a multiloculated sac which retains the shape of the kidney, is formed. Intermediate types may occur, depending on anatomical variations in the relationship of the kidney to its pelvis.

As a hydronephrotic kidney increases in size it does so in the direction of least resistance, therefore it projects towards the peritoneum which forms an investment for its anterior surface. On the right side it tends to displace the hepatic flexure downwards and medially but on the left side the splenic flexure maintains its attachment to the parietes. It is very exceptional for a hydronephrosis to exert harmful pressure on the abdominal organs.

A hydronephrosis is said to be open when urine escapes from it and "closed" when the outflow ceases. An open hydronephrosis is liable to become completely obstructed from time to time. This may be determined by the intake of large draughts of fluid and it may give rise to attacks of pain in the loin and enlargement of the kidney.

At cystoscopic examination it is often noted that the hydronephrotic kidney secretes more copiously than the healthy one, as is evidenced by more frequent ureteral contractions, but the urine is more dilute. In more advanced cases the escape of urine may be very infrequent and when obstruction is absolute ureteral contractions cease. When a ureteral catheter is passed large quantities of urine are often withdrawn and on injecting fluid into the renal pelvis its capacity may be found to be greatly increased. In a large hydronephrosis the opaque fluid injected for diagnostic purposes may be so greatly diluted by the fluid contents of the sac that no shadow may be portrayed radiographically.

A hydronephrotic kidney on account of its size is more liable to injury than a normal one. Spontaneous rupture is recorded.

### STRICTURE OF THE URETER

Stenosis of the ureter may be of congenital origin or it may be an acquired condition due to pathological processes affecting its walls.

Congenital stenosis is relatively uncommon and autopsy examination of 1 200 infants by Englisch (in Vienna) showed that it was present

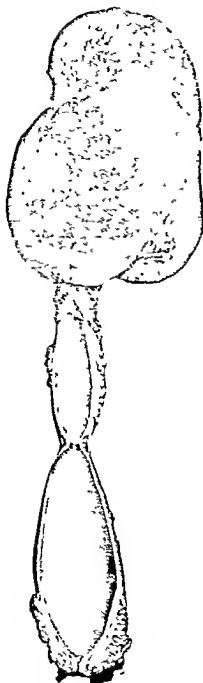


FIG. 272. Hydronephrosis and hydro-ureter due to a fibrous stricture at the lower end of the ureter.

(By courtesy of the late Mr D. S. Middleton.)

in 65 cases; the stenosis was situated at the upper end of the ureter in 34, at the lower end in 28, and about the middle of the ureter in 3. The stenosis may be due to persistence of a valve or fold of mucous membrane or to narrowing of a segment of the ureter. Any part of the ureter may be affected, but the commonest situations for such abnormalities are at the upper end, at the entrance to the bladder, and at the point at which the ureter enters the pelvis minor. The degree of ureteral obstruction is very variable, but in some it is sufficient to lead to hydronephrosis.

Acquired strictures of the ureter are very rare. They may result from cicatrization of an ulcer caused by an impacted calculus, from injury at operation, and from the infiltration of the ureteral wall by a malignant tumour of the colon or of the female pelvic organs. Occasionally ureteral strictures are found in association with long-standing infection of the lower urinary tract, especially in association with urethral stricture. Strictures of the ureter have been observed after childbirth (so-called puerperal strictures). They are commonest on the right side and in the pelvic portion of the ureter near its termination in the bladder. They are believed to result from injury to the wall of the ureter in parturition, with subsequent repair by scar tissue. The hydro-ureter of pregnancy predisposes to their formation (*see p. 616*).

The ureter at the site of a stricture is indurated by scar tissue. Usually all coats are involved and the muscle is replaced by fibrous tissue. Peri-ureteral fibrosis may fix the ureter to the peritoneum. The lumen of the ureter at the stricture

is reduced and its epithelium is often of a squamous character. The ureter above the stricture is dilated and slightly hypertrophied and may be tortuous. Stricture of the ureter tends to cause obstruction of urinary outflow and hydronephrosis, and the stagnation of urine renders the kidney more vulnerable to infection especially by *Bacillus coli* so that pyelitis is a common complication.

**Ureterocele** Ureterocele or ballooning of the intravesical portion of the ureter into the bladder is a rare condition. The most important predisposing cause is narrowing of the ureteral orifice of either congenital or acquired origin. The prolapse may lead to interference with renal drainage. In the advanced stages the ureterocele sac may be very large and may cause blockage of the urethra during micturition. In women it may traverse the urethra and present at the vulva and give rise to incontinence.

## PYOGENIC INFECTION OF THE KIDNEYS

The principal pyogenic infections of the kidney of surgical importance are (1) *Pyelitis*, in which the inflammation is chiefly restricted to the mucous membrane of the renal pelvis (2) *Pyelonephritis* in which the inflammation involves both the renal pelvis and the parenchyma of the kidney (3) *Pyonephrosis* in which there is an added factor of obstruction to the outflow of urine and (4) *Hæmatogenous suppurative nephritis*.

### Pyelitis

This is a common infection. It affects women far more often than men and it is especially common as a complication of pregnancy affecting especially the right kidney.

Pyelitis may arise acutely and after a short period may undergo resolution or it may arise insidiously and pursue a chronic course.

Acute pyelitis is often sudden in onset and may be accompanied by severe constitutional disturbance. Since the urine is highly acid it may give rise to scalding pain on micturition.

The pathological state is not fully understood since for obvious reasons the opportunity rarely offers of examining a kidney in a state of simple pyelitis. It is presumed however, that there is an inflammatory reaction which is mainly evident in the mucous membrane of the renal pelvis. Probably in all cases the renal parenchyma shares, to a limited extent, in the pathological changes.

Chronic pyelitis may arise insidiously or may occur as a sequel to acute pyelitis. It is a common condition, and may be responsible for much chronic disability associated with pain over the affected kidney and frequency of micturition. The pathological changes are those of a chronic inflammation. The mucous membrane of the renal pelvis is thickened and somewhat pale in colour, or in some cases it is thin and atrophic. The muscle coat of the renal pelvis and ureter is atrophic, and this change may lead to mild degrees of hydronephrosis, sometimes accompanied by dilatation of the ureter.

In some cases in response to the chronic irritation the mucous



membrane of the renal pelvis undergoes proliferative changes and assumes a squamous-cell character—*leukoplakia of the renal pelvis*. This change which is distinctly rare, has sometimes been found in kidneys containing calculi presumably the result of the chronic irritation. Leukoplakia of the renal pelvis is regarded by some as a pre-cancerous lesion.

**Ætiology of Pyelitis.** The infecting organism in pyelitis is generally a coliform bacillus but the factors that determine its localization in the renal pelvis are not yet definitely established. It is well known that an apparently healthy kidney may allow organisms to pass from the blood stream into the urine and it is established that *B. coli* is often excreted in this way. It seems probable therefore that in pyelitis the infection is hæmatogenous and that the determining factor is some local lesion which renders the renal pelvis unduly susceptible. Occasionally there is some obvious local lesion such as a stone or a malformation of the kidney. In pregnancy pressure upon the right ureter by the enlarging uterus or hydro-ureter from other causes (see p. 616) may as a result of urinary stasis predispose to pyelitis.

Whilst the view generally held is that given above it must be admitted that the organisms are derived from the colon and reach the kidney by way of the lymph vessels. Such a theory would explain the frequency of pyelitis in women who are especially liable to colon sepsis and in the right kidney which is in close relation to the proximal colon.

### Pyelonephritis

Here the infection attacks the renal parenchyma as well as the mucous membrane of the pelvis. The disease may be unilateral or bilateral depending upon its manner of causation and in either case it is considerably more serious than pyelitis. Clinically it is associated with a high temperature, rigors and great toxæmia and often it leads to uræmia and ends fatally.

The kidney becomes swollen, engorged with blood and of a purple colour. At first, the inflammatory change is most obvious in the mucous membrane of the pelvis and calices which are intensely hyperæmic and œdematous. Later small abscesses appear in the parenchyma of the kidney first near one extremity of the organ later in other parts. Extending from the pelvis to the cortex there are numerous faint greyish yellow streaks of suppuration which mark the spread of infection between the tubules of the medulla towards the capsule. Later the abscesses increase in size and may become confluent or open at the renal pelvis or they may spread towards the surface of the kidney and lead to suppuration in the perinephric tissues.

**Ætiology.** The infecting organisms in pyelonephritis are generally mixed. Coliform bacilli are often present along with staphylococci, streptococci and sometimes *B. proteus* and other organisms. In some cases the infection appears to be hæmatogenous and its onset may be determined by pre-existing disease of the kidney for example by nephrolithiasis or a tumour. In such circumstances pyelonephritis may

be unilateral, though it is very apt to become bilateral. In the majority of cases, however, the infection is derived from the lower urinary tract, whence it reaches the kidney, along the ureter or more probably, by way of the peri-ureteral lymph vessels. This ascending type of infection generally follows septic cystitis (*consecutive suppurative nephritis*), and is especially apt to occur when there is an obstruction to the outflow of urine, for example, by enlargement of the prostate or by stricture of the urethra. Such an obstruction affects both kidneys, and consequently pyelonephritis of this type is generally bilateral. The ascending infection is especially apt to follow operations on the bladder even the passage of instruments.

### Pyonephrosis

In this condition there is a primary infection of the kidney and renal pelvis, and, in addition, a partial or complete obstruction to the outflow of urine, often due to calculi. Pyonephrosis is to be distinguished from infection of a pre-existing hydronephrosis, though in the later stages the two conditions are somewhat similar.

The infection in pyonephrosis is generally mixed. Coliform bacilli usually predominate, and give the pus a characteristic odour, and staphylococci, streptococci and *B. proteus* are often present.

The obstructing agent usually is a stone (*calculous pyonephrosis*) or less often a tumour of the kidney or renal pelvis. The stone is often of large size, filling the renal pelvis. In other cases a small stone is responsible, by obstructing the ureter or the pelvi-ureteral junction. Occasionally a stone obstructing one of the major calyces gives rise to pyonephrosis limited to one part of the kidney.

As a result of the infection the mucous membrane of the pelvis and calyces becomes inflamed and ulcerated. The parenchyma of the kidney becomes thinned by pressure and necrosis. Such parenchyma as remains is infiltrated by inflammatory products and often riddled with small abscesses. The pelvis and calyces are greatly dilated, and contain pus mixed with alkaline, ammoniacal urine. Often there are secondary phosphate concretions.

The renal pelvis is generally dilated, but rarely to the same extent as in hydronephrosis, for the thick, inflamed wall resists distension.

Usually the obstruction to the outflow from the kidney is not complete, and consequently the urine contains quantities of pus and is generally foul smelling. Complete obstruction may supervene, however, and then the pyuria becomes less obvious, and coincidentally the kidney becomes larger and more tender, and the constitutional effects become aggravated.

### Hæmatogenous Suppurative Nephritis

In septicæmia and in pyæmia multiple small abscesses may develop in the kidney. They vary in size from a pin's head to a cherry. They are usually situated in the renal cortex.

Staphylococcal infection of the kidney is an occasional complication of such lesions as furunculosis, carbuncle and osteomyelitis. It occurs

in adults and is nearly always unilateral and in a number of cases, is preceded by trauma to the kidney. The resulting lesion may take the form of an acute abscess in the cortex, but more often the suppurative process is subacute and is associated with multiple areas of necrosis—which if aggregated form the *carbuncle of the kidney*. In the early stages there are multiple opaque foci in one part of the cortex; later these may fuse and give rise to a localized enlargement of the kidney. A perinephric abscess results from the outward extension of the suppurative process, but eruption into the renal pelvis is exceptional.

This form of renal infection pursues a subacute course. It is attended by rigors, sweating and pain in the loin, and there may be considerable emaciation. Urinary symptoms are generally absent, and as the inflammatory process begins in the cortex of the kidney and remains confined to it, pus and organisms are not found in the urine. A perinephric abscess may be the most obvious feature and then the renal origin of the infection is often overlooked or it is not suspected.

### TUBERCULOSIS OF THE URINARY TRACT

Tuberculous infection of the urinary tract is a local manifestation in a tuberculous subject, the result of a systemic infection. The primary source of infection, which may be active or quiescent, is either in the lung or less often a lymph gland. Evidence or a history of tuberculous disease elsewhere is forthcoming in at least 75% of cases and in the male sex, genital tuberculosis affecting the epididymus is present with considerable frequency.

The primary lesion in the urinary tract is almost invariably situated in one kidney, and since there is usually no evidence of hæmatogenous infection in other organs, it is generally presumed to be due to a solitary embolus of tubercle bacilli set free in the blood stream. It seems possible, however, that in some cases at least, the renal lesion is due to the lighting up of a latent miliary focus.

Once established in the kidney, the disease tends to spread throughout the urinary tract and eventually, if unchecked, involves the ureter, the bladder and the remaining kidney. The mode of spread of tuberculosis in the urinary tract has been the subject of much speculation. It seems almost certain that the disease spreads from the kidney down the ureter to the bladder by direct continuity of tissue along the mucous membrane and also in the periureteral lymph vessels. It has been suggested that the bladder may be infected by organisms carried down in the urine, but this seems unlikely. The remaining kidney may be involved by further hæmatogenous infection or by infection ascending from the bladder. Such an ascending infection may be conceived to occur by direct spread along the mucous membrane of the ureter, by way of the periureteral lymphatics or possibly even as a result of regurgitation of infected urine from the contracted bladder. In most cases it seems likely that spread by continuity of tissue is responsible.

#### Tuberculosis of the Kidney

Excluding acute miliary lesions, renal tuberculosis takes a chronic course. Although hæmatogenous it is almost always confined at first

to one kidney, and probably in about 80% it remains unilateral for several months or even years

The earliest focus lies in the cortex near one or other extremity of the kidney, rarely at its mid part. By extension and ulceration the disease reaches the mucous membrane of a neighbouring calyx whence it spreads to other parts of the renal pelvis. The renal parenchyma is invaded by tubercles at first discrete later confluent and eventually the capsule is reached. Occasionally a cold abscess develops in the perinephric fat.

It is important to recognize that all the early changes occur principally within the substance of the kidney and that the disease may be advanced before there are notable changes in the urine or other pathological evidence of significance.

**Gross Appearance** In most cases the kidney is widely involved. The perinephric fat is oedematous matted and adherent so that the kidney is exposed with some difficulty. There may be tiny tubercles under the capsule or the surface may be raised in large nodular protuberances while the kidney feels indurated or soft and perhaps fluctuant.

On section of the extirpated kidney the extent of the disease is seen to vary in different parts being usually most advanced near the renal pelvis at one extremity (see Fig 273). The pelvis is usually ulcerated and its wall replaced by granulation tissue. When the disease is extensive the parenchyma is partly replaced by cavities which are lined by caseous matter and granulation tissue and contain thick white pus. Extending towards the cortex are yellow lines which indicate secondary pathways of extension and scattered throughout the kidney there may be many discrete tubercles.



FIG 273 Tuberculosis of the kidney. The kidney is greatly enlarged. There are several cavities lined with tuberculous granulation tissue communicating with the renal pelvis and all the calyces are affected by the ulcerative process. Numerous small tubercles are seen in the cortex and medulla and in the mucous membrane of the renal pelvis.

(Department of Surgery, University of Edinburgh)

The wall of the ureter may be thick, infiltrated with tubercles, and fibrotic its epithelial surface ulcerated and rough. The lumen of the ureter is sometimes obliterated by fibrosis, but often is dilated, forming a thick walled irregularly tortuous tube.

**Special Types of Lesion** In typical cases the progress of the disease is as described above and the lesion may be designated *tuberculous pyelonephritis* (see Fig 2-3). In other cases the progress is modified and

other types of lesion may be recognized. If the ureter should become completely obstructed and the disease is of milder type, the pelvis and calyces become dilated with turbid watery fluid—*tuberculous hydronephrosis*. Sometimes a slow caseous process spreads through the entire kidney, which becomes a functionless multilocular sac completely filled with solid cheesy material—*tuberculous pyonephrosis* or *caseous kidney* (see Fig 2-4). In these cases the ureter is often occluded but since all secreting tissue is already destroyed the pelvis is not dilated but remains small. At this stage the disease not uncommonly becomes arrested, bacilli disappear from the urine and the symptoms subside. Such a sequestered caseous mass often undergoes partial calcification, and on radiography casts a dense, irregularly mottled shadow.

**Significance of "Tuberculous Bacilluria."** It has often been observed in the course of progressive tuberculosis of any part of the body that the urine contains tubercle bacilli yet the kidney, subsequently examined at autopsy, appears unaffected hence it has

FIG 2-4 Caseous tuberculosis of the kidney (tuberculous pyonephrosis). The renal pelvis is small and the ureter is occluded. The entire secretory tissue is replaced by large cavities containing caseous material. (Department of Surgery, University of Edinburgh.)

been inferred that the kidney may excrete tubercle bacilli, yet remain free from disease. The accuracy of this observation, however, has been rendered very doubtful by the extensive researches of Medlar, who showed that by careful search tubercles are always to be found in such kidneys though sometimes only after prolonged examination of serial sections.

Nevertheless, the fact remains that the presence of bacilli in the urine is quite consistent with the absence of any gross lesion, an observation that emphasizes the difficulty of basing diagnosis solely on urinary examination.

### Tuberculosis of the Bladder

Usually the bladder is infected from the kidney and ureter, less often from the seminal vesicles or the prostate

When derived from the kidney, the vesical infection begins at the corresponding ureteral orifice, and spreads thence over the trigone, and ultimately to the fundus. The earliest sign is œdema of the lips of the ureteral orifice, in a short time this area becomes congested, and later small ulcers appear, which are shallow and hæmorrhagic with adherent tags of blood clot and pus, eventually tubercles may be recognizable, though this is rare. Since the muscle of the ureteral wall is extensively involved it fails to contract during the passage of urine, and consequently one of the early signs visible on cystoscopy is the cessation of the normal rhythmical contraction and parting of the lips of the orifice. Later, cicatricial contraction of the ureter causes retraction of the corresponding corner of the trigone, and the orifice forms a gaping circular pit—the so called golf hole ureter.

As the disease progresses, the bladder wall becomes infiltrated with inflammatory exudate and cells, it becomes thickened contracted and inelastic, and its capacity is reduced from the normal of 300 c cm to as low as 50 c cm. As a secondary effect, a certain degree of "back pressure" may develop, and may lead to hydronephrosis. This complication affecting the function of the second kidney, is naturally of serious import.

### TUMOURS OF THE KIDNEY

Malignant tumours of the kidney belong to two principal classes (1) the adenocarcinoma or hypernephroma—a tumour affecting adults and arising in the renal parenchyma (2) the adenosarcoma (mixed or embryonic tumour) of infants and young children.

Tumours arise also from the epithelial lining of the renal pelvis (see p 632)

#### Adenocarcinoma, Hypernephroma

Practically all malignant epithelial tumours arising in the renal parenchyma conform closely to one general type of striking appearance characteristic morphology, and uniform behaviour. They are bulky irregularly lobulated tumours, which may be firm solid and of grey or yellow colour, but often undergo softening cyst formation and discoloration by extravasated blood. They invade the kidney substance gradually and show a great tendency to metastasize by the blood stream.

In the past attempts have been made to distinguish in this group two varieties—*hypernephroma*, of adrenal origin and *adenocarcinoma* derived from the tubules of the kidney. The distinction has been made principally upon histological grounds according as the tumour resembles the adrenal cortex or contains tubules and papillæ more suggestive of a renal origin. It seems probable, however, that this distinction has little foundation and should be discarded. Variations

imperfect capsule of condensed renal tissue, and broad fibrous trabeculae subdivide it into numerous lobules. Near its centre the tumour is often solid, of firm consistence and bright yellow colour. Around this central core the tumour is partly solid, partly excavated by cyst-like spaces, some of which are bright yellow, whilst others are discoloured to various shades of orange and red.

**Microscopic Appearance.** This varies somewhat in different tumours and in different parts of the same tumour, but the general picture is a fairly characteristic one. The cells superficially resemble those of the adrenal cortex, being cuboidal or columnar, though often modified in shape by mutual pressure. Their nuclei are small, rounded and deeply stained; their cytoplasm is abundant and either clear or slightly granular. In the fresh state, before being subjected to fat solvents, the cells are filled with a soluble material containing glycogen, cholesterol, and fats. They are disposed in sheets or in long columns, or in solid masses, bounded by delicate trabeculae or connective tissue. The columns of cells are intimately related to blood vessels, which are large and thin-walled. Generally, the cellular masses are solid, with no visible acini, but sometimes there are irregular spaces, tubular clefts or papillary formations.

**Spread of the Tumour.** The tumour progresses slowly at first, but finally it encroaches upon the calyces of the renal pelvis, and leads to hæmaturia. The quantity of blood lost is often considerable and clots may form in the renal pelvis, causing colicky pains during their descent within the ureter.

Tumours of the kidney have a remarkable tendency to spread along the lumen of the renal vein, which is sometimes choked by tumour tissue, and the growth may extend by continuity, even into the heart and lungs. Rarely a mass in the left renal vein obstructs the testicular vein and leads to a certain degree of varicocele and to pain in the testis.

**Distant metastases**

develop most often in the lungs and in bones. Pain in the chest or hæmoptysis, or a pathological fracture due to a bone metastasis, may



FIG 276 Adenocarcinoma (hypernephroma) of the kidney.  $\times 110$  The tumour is composed of solid masses of cells, with small, deeply staining nuclei and abundant clear protoplasm. Note the large thin-walled blood space.

(Laboratory of Royal College of Physicians of Edinburgh.)

be the first indication of the malignant process. Not infrequently a single metastasis appears at a moderately early stage of the disease some time before general dissemination occurs.

**Nature of the Tumour.** The nature of the tumour has been a much debated subject. Until comparatively recent years the field has been held by the theory of von Grawitz who considered that the tumour is of adrenal origin—a hypernephroma—and that it arises from displaced portions of adrenal tissue within the substance of the kidney. This theory is based upon two principal considerations: (1) that “rests” of adrenal tissue are present sometimes under the capsule or in the cortex of the kidney; (2) that tumours of this type closely resemble adrenal tissue in their gross appearance, in their architecture and in the characteristics of their individual cells.

Von Grawitz's theory has been assailed on numerous occasions, and Nicholson in a masterly review of the whole subject, brought convincing evidence against it which may be summarized as follows: (1) adrenal rests are not confined to the kidneys, but occur often in the broad ligaments, in the retroperitoneal tissues and elsewhere, whereas

hypernephromata are almost invariably intrarenal, (2) the architecture of these tumours is no indication of their origin but results from the mutual pressure of swollen hydropic cells, (3) the individual cells—with their content of glycogen and fat—though very like adrenal cells are not unlike cells in other situations, (4) true tumours of adrenal

cortex arising in the adrenal gland, almost always have a very obvious effect upon the secondary sexual characteristics and lead to sexual precocity with virilism whereas no such biological action has been observed in association with such a tumour in the kidney.

As a compromise between these opposing views, many attempts have been made to identify different types of tumour, some of adrenal others of renal origin but such a subdivision as has already been pointed out, is beset by many difficulties and has not been widely adopted. At pre-



FIG. 277. Adenocarcinoma (hypernephroma) of the kidney.  $\times 400$ . The tumour is composed of solid masses of large rounded cells with small nuclei and very clear protoplasm. On the left is a thin walled blood vessel.

(Laboratory of Royal College of Physicians of Edinburgh.)

rates to the general opinion favours the view expressed by Nicholson that the hypernephroma is an adenocarcinoma derived from cells of the renal tubules.



## Renal Adenosarcoma (Nephroblastoma)

This rare tumour occurs in childhood, practically never after the seventh year. It forms a rounded or nodular mass, which may attain great size, replacing the entire kidney, displacing the viscera and expanding the whole abdomen.

The tumour arises in the substance of the kidney and is of bluish-white or pale grey colour. The blood supply is poor, with scanty thin-walled vessels, and consequently the tumour is liable to undergo necrosis with hæmorrhages, zones of softening, and the formation of cyst-like cavities.

The tumour is not encapsuled, and it invades the renal parenchyma and destroys it, so that in the later stages little trace of normal tubules may remain. The ureter when traced upwards, merges into the tumour mass. The renal pelvis is compressed and obliterated but its cavity is not actually invaded, and consequently hæmaturia and other evidence of urinary disorder are frequently lacking.

The tumour spreads by direct invasion of adjacent structures to the peritoneum, omentum, and retroperitoneal tissues. Occasionally secondary deposits appear in the opposite kidney, in the lungs or other viscera.

The microscopic structure is that of a mixed tumour in which sarcomatous elements preponderate. The greater part of the tumour is made up of round or spindle-shaped cells, lying in a scanty delicate matrix, but in places there are gland-like collections of columnar or cubical cells arranged in irregular acini, and occasionally there are islands of cartilage and of plain muscle fibres.

The origin of the tumour is not clear. It is generally accepted that the tumour is derived entirely from mesoderm, from some misplaced embryonic rudiment. Some authorities have ascribed it to vestiges of the mesonephros or of the metanephros, but its structure suggests an even earlier origin. According to Wilms, it is derived from misplaced portions of a myotome, or primitive body segment, which normally gives rise to a whole excretory apparatus.

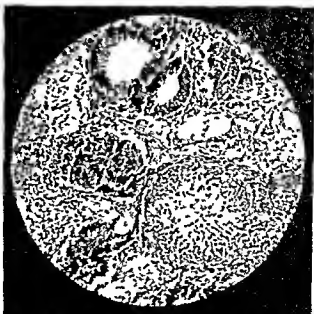


FIG. 278. Nephroblastoma.  $\times 150$ . Columnar cell acini are set in a stroma of spindle cells.

(By courtesy of Prof. J. W. S. Blacklock.)

(see p 622) In about 50 % of the cases on record the carcinoma has arisen as a complication of renal calculus

### TUMOURS OF THE URETER

Primary tumours of the ureter are exceptionally rare In general they resemble the epithelial tumours of the renal pelvis, and papilloma papillary carcinoma and epidermoid carcinoma are recognized They may be responsible for intermittent or persistent hæmaturia and may lead to hydronephrosis

Secondary tumours of the ureter are more common The ureter is invaded frequently by tumours of the cervix uteri, colon, bladder or prostate, or by metastatic growths in the retroperitoneal or pelvic lymph glands Occasionally the ureter becomes the seat of secondary growths from tumours of the renal pelvis

### URINARY CALCULUS

This is an age old disease, and its history goes back to the earliest periods of civilization Urinary stones were known to the ancient Egyptians, and have been found in mummies several thousand years old, and the operation of "cutting for stone" was practised several centuries before the Christian era It would appear that at present the incidence of stone in the bladder is steadily decreasing, and in Britain this condition is much less prevalent now than during last century The frequency of stone in the kidney and ureter, on the other hand, has shown an apparent increase, which is doubtless accounted for by improved methods of diagnosis

**Mode of Formation of Calculi** The urine contains a number of crystalline substances, which are held in heavily supersaturated solution through the protective action of colloids, such as mucin and chondroitin sulphuric acid Under certain circumstances the crystalloids are precipitated, and if at the same time the colloids become modified losing their solvent action and acquiring a kind of adhesive property, the precipitated crystals are bound together to form stones

Thus it may be stated as a general principle that urinary stones are composed of crystalloid particles bound together by colloids The two elements, *crystalloid* and *colloid*, are equally essential, for crystalloids alone, when precipitated, pass freely to the exterior, and for calculus formation the adhesive properties of colloids are required

It is believed that in renal stone formation the process begins within the kidney substance According to Randall a 'primary renal stone' (i.e., one for which no predisposing factors are demonstrated) is formed by the deposition of urinary crystals on a plaque of calcium deposited within the substance of a renal papilla, while "secondary" stones (those with a recognized predisposing factor, e.g., hyperparathyroidism) originate as deposits within the collecting tubules

**Predisposing Factors** Increase in the urinary calcium output is one of the most important of the known predisposing factors It may

be due to excessive intake in the diet (or to a low phosphorus intake) and this may be one of the factors determining the geographical incidence to increased absorption of calcium by the intestines under the influence of excessive administration of Vitamin D or to skeletal decalcification from prolonged decubitis or in parathyroid osteitis or other bone-rarefying diseases.

Infection of the urine is a well-established predisposing factor in relation to certain types of stones particularly phosphatic stones. The infecting agents include urea-splitting organisms such as staphylococcus aureus and also B. proteus and others. Infection may lead to stone precipitation by altering the solubility of calcium in the urine and possibly also as Hewitt has shown to occur in cultures on calcium rich agar medium, by the formation of bacterial calculi in which the organisms are adsorbed in an inorganic matrix due to the combination of calcium absorbed on the bacteria with ammonium carbonate resulting from the bacterial nitrogenous metabolism.

Stasis of urine is recognized as a factor predisposing to stones which are thus common in the bladder behind an enlarged prostate or a urethral stricture or in malformations such as a horse-shoe kidney. High concentration of the urine due to excessive sweating may be one of the factors responsible for the high incidence of stones in tropical countries.

Vitamin A deficiency has been shown by McCarrison to give rise to stone formation in experimental animal and may be a factor of importance in countries where the diet is inadequate in respect of this substance. It probably acts partly by diminishing the resistance to infection and partly by inducing keratinization of the urinary epithelium.

Finally the citrate content of the urine has recently been claimed to have some importance in view of its function as a solvent of calcium. The amount of citrate excreted varies with the output of calcium, owing to their close relationship in osseous tissue. The urinary citrate also varies with the hydrogen-ion concentration, being higher in alkaline than acid urine and it varies at different phases of the menstrual cycle being raised by oestrogens. The significance of these variations is not yet completely understood.

### Types of Calculi

It is necessary to distinguish two principal varieties, primary and secondary stones. *Primary stones* are those that arise in an apparently healthy urinary tract and that are composed of substances present in the urine normally or as a result of metabolic disorders. Primary stones occur in acid urine. They require no preformed nuclei, but appear to arise from the slow precipitation of crystals in a colloidal magma. Primary stones are usually composed of oxalates or of uric acid, rarely of cystine. *Secondary stones* are those that result from inflammation—bacterial or aseptic—and their formation requires a preformed nucleus, which may be a primary stone, a foreign body, a clump of organisms, or a mass of inflammatory exudate. Since their development depends

upon the liberation of ammonia from urea, they are found in alkaline urine. Secondary stones are almost invariably composed of ammonium magnesium phosphate (triple phosphate).

**Oxalate Calculi** Calcium oxalate is a normal constituent of the urine, approximately 15 to 20 mgm being excreted daily in health. It is derived principally from the food, and after the ingestion of foods rich in oxalates it may be precipitated from the urine in crystalline form. Of the foods rich in oxalates the most common are rhubarb, spinach and asparagus, strawberries are of ill repute in this respect, but without reason, for their oxalate content is less than that of potatoes. The absorption of oxalates from food depends to some extent upon the gastric acidity, and patients who suffer from hyperchlorhydria are especially prone to oxaluria.

Oxalate calculi are extremely hard. They may be smooth and rounded, or nodular like mulberries. Often they are of irregular shape and covered with sharp spicules. These physical characteristics modify the course and effects of oxalate calculi. The stones arise in the renal pelvis or calyces and like other small stones similarly placed they are liable to be propelled down the ureter, but whereas stones of other composition usually pass rapidly into the bladder the rough surfaced oxalate stones frequently become impacted in the ureter. In any position they irritate the mucous membrane and excite an outpouring of lymph and blood which renders them black or dark brown. The irritation is apt to lead to infection or to degenerative changes in the kidney, and the outpouring of lymph or inflammatory exudate favours secondary deposition of layers of phosphatic material.

**Calculi of Uric Acid and Urates** Almost 1 mgm of uric acid is excreted daily in the urine. It is partly of exogenous origin, from meat and other foods and partly endogenous from the breaking down of tissues. In the lower animal kingdom and in birds and reptiles, uric acid forms the chief vehicle for excretion of nitrogen, but in higher animals and in man this function is assumed principally by urica.

Stones of uric acid and urates may arise in the renal pelvis or the bladder. They are hard but smooth, yellow or brown in colour, and usually rounded or oval. They may attain large size, and if situated in the renal pelvis may become moulded to the shape of that cavity. Stones are rarely composed of uric acid alone, commonly there is an admixture of urates, and not infrequently there are traces of calcium oxalate. Occasionally in children stones are composed chiefly of ammonium urate, they are yellow, soft and friable.

**Cystin Calculi** Cystin calculi, though uncommon, are of especial interest from their close relationship to a metabolic disorder. Cystin is an amino acid with a high sulphur content, in normal subjects the sulphur is oxidized completely and is excreted as sulphates, but in a small proportion of persons some "inborn error of metabolism" causes the cystin to appear in the urine unchanged. In the urine it is deposited as flat, colourless hexagonal crystals easily recognized on microscopic examination. After the urine has stood for some time the sul

phur may become combined as hydrogen sulphide, and this is recognizable by its smell

Cystinuria is usually a familial disorder and may be present throughout life. Only a small proportion about 2% of the subjects of cystinuria develop stones but in this small minority the tendency is very great. The stones often appear in childhood and are multiple and after their removal by operation others tend to form. They are moderately hard with smooth surface and of yellow waxy appearance. On exposure to light and air they gradually darken to an olive green colour. Cystin stones usually form in the renal pelvis and calyces, and when small they readily pass down the ureter to the bladder.

**Phosphatic Calculi** Normal urine contains phosphates derived from the breaking down of tissues rich in phosphorus and to a less extent from absorption in food, but phosphatic stones are not composed of these substances but of triple phosphate (ammonium magnesium phosphate) of which only a trace is normally present. The conversion of the phosphates present in health into triple phosphates depends upon the liberation of ammonium carbonate from urea and as this process is often due to the decomposition of urea by micro-organisms it follows that phosphatic stones are frequently the result of a urinary infection.

Phosphatic stones are grey or of a dirty white colour and may be moderately hard or soft and friable. They are always deposited around some preformed nucleus such as a primary oxalate or urate stone or a foreign body. Often they attain large size and they form the majority of stag horn and other large irregular calculi in the kidneys, ureter or bladder. Moreover since they often arise from staphylococcal or streptococcal infections that resist treatment recurrence after operation is common. The second kidney also may become affected.

**Rare Constituents of Stones** Xanthin like cystin is a product of abnormal metabolism but stones containing more than a trace of xanthin are excessively rare. Calcium carbonate often takes part in the formation of phosphatic calculi and may rarely be the predominant constituent of a stone. Indigo derived from indol is occasionally found and if present in quantity it may impart its colour to the stone. So called *fibrin stones* small putty like masses found in grossly infected kidneys arise from the inspissation of old blood clot or an inflammatory exudate. Rarely bacteria form the principal constituents of small soft concretions.

### Stones in the Kidney

The majority of urinary stones are formed in the kidney. They are usually single less commonly multiple and are formed in the calyces or in the renal pelvis never in the parenchyma. Usually they lie in the lower major calyx and may remain there through life or they may travel to the ureter and the bladder. The stones may retain their purity, but often from irritation and inflammatory change they become coated with phosphates. At first a renal calculus is rounded or

oval, but in its growth it may become moulded to the shape of a calyx or a portion of the renal pelvis, phosphatic stones often form a complete cast of the pelvis and calyces—the so called stag horn stone

Any renal calculus, but especially one associated with obstruction to the flow of urine, may lead to gross pathological changes in the kidney—interstitial fibrosis, hydronephrosis, pyelonephritis and pyonephrosis. Of infective complications those from staphylococci and streptococci are the most dangerous, for these are urea splitting organisms which render the urine alkaline and lead to extensive phosphatic precipitation. Not infrequently also the organisms tend to infect the other kidney and to produce similar changes there

### Stones in the Ureter

Stones in the ureter always originate as renal stones which have been arrested during descent, and they are usually oxalate stones which, from their irregular shape, are particularly liable to become impacted. Impaction usually occurs at one of the sites of normal narrowing near the entrance to the bladder, at the crossing of the iliac vessels or at the pelvi ureteral junction (in that order of frequency). When impacted, a stone ulcerates the mucosa, so that it may lead to subsequent fibrosis. Sometimes the ulcer deepens so that the stone comes to lie in a pocket in the perireteral tissues, and no longer obstructs the flow of urine. At first a ureteral stone maintains its original shape and composition, but it rapidly becomes encrusted with phosphates, and it then becomes elongated, conforming to the shape of the ureter.

Sometimes the ureter is completely obstructed but usually a certain amount of urine can reach the bladder, in either case the ureter above dilates and hydronephrosis develops. If the obstruction is not soon relieved the renal parenchyma becomes thinned out, fibrous and functionless. Experimentally, it is found that the kidney will not recover after a complete obstruction of longer than two or three weeks, particularly is this so if the other kidney is able to compensate for the loss, but if the second kidney is diseased the first may recover to some extent (renal counterbalance).

If a stone lies in the ureter without causing much obstruction there may sometimes be an increased flow of urine from that side, possibly from reflex stimulation or more probably from chronic interstitial change in the kidney. A ureteral stone causes colicky pains during its descent, and dull pains in the loin from over distension of the renal pelvis. It may give rise also to local pain in the lower quadrant of the abdomen, and on the right side this with reflex boarding of the muscles may simulate appendicitis. Frequency of micturition may be present, from irritation of the ureter and consequent reflex stimulation.

### Stones in the Bladder

Stones may originate in the bladder or they may reach it from the kidney. As in the kidney, stones originating in the bladder may be of primary or secondary type. Primary stones may form in a perfectly

healthy bladder, but are rather more common where there is some obstruction to the passage of urine from prostatic enlargement or other cause. Secondary stones are much more common especially when cystitis is present. They are composed principally of triple phosphates deposited upon a nucleus such as a primary stone or a mass of inflammatory exudate. In rare instances the nucleus is formed by objects introduced along the urethra and hairpins lead

pencils or even portions of catheters have been responsible. Similarly ligatures of catgut or silk may be responsible.

Not infrequently large stones resulting from secondary deposition on a primary calculus are laminated and layers principally composed of phosphates alternate with those of other substances. A classical example was the stone of Napoleon III which consisted of laminae of uric acid alternating with phosphates. At that time all stones were thought to arise from disordered metabolism and the alternation of laminae was believed to follow changes in the amount of purin bodies or of phosphates consumed at different times, the layers of uric acid were attributed to the ample



FIG. 280. Multiple renal calculus composed of uric acid and urates. A calculus of similar composition impacted at the pelvic ureteral junction had led to hydronephrosis.

(Department of Surgery, University of Edinburgh.)

dietary of the Paris season and the phosphatic deposits to the waters of Vichy consumed during the annual cure. A more probable explanation however though less picturesque is that the phosphatic laminae were attributable to recurring exacerbations of cystitis.

### Stones in the Urethra

Stones in the urethra are usually migratory stones that have passed from the kidney or bladder. They lodge in the urethra near one of the sites of normal narrowing either in the prostatic urethra or close to the external meatus. When impacted they become coated with phosphates and assume an elongated shape. Occasionally stones

originate in the urethra, but only in the presence of a stricture and infection. They obstruct the flow of urine and lead to bilateral hydronephrosis, often with infection. Sometimes the stone ulcerates through the urethral mucosa and comes to lie in a shallow diverticulum and it may lead to extravasation of urine and to a fistula. Occasionally a stone impacted in the female urethra may ulcerate into the vagina, and may remain there for many years. Such a stone (the so called vaginal stone) may attain considerable size from the accretion of phosphates, and may assume an elongated shape. A radiogram may demonstrate a central laminated portion, the source of the stone.

### ANURIA

Anuria—the arrest of secretion of urine—may occur in many different circumstances, and, according to the nature of the conditions causing it, three types are recognized (1) pre renal, (2) renal, and (3) post renal.

(1) *Pre renal anuria* is usually due to circulatory changes that interfere with filtration of fluids from the blood as it passes through the glomeruli. The blood pressure in the glomerular vessels is normally about 90 mm of mercury, and if the general arterial pressure falls far below this level renal secretion ceases.

Pre renal anuria arises in any state associated with sustained reduction of blood pressure, for example, in severe shock, or in anhydremia from excessive loss of fluids by the skin or bowel. It may occur after spinal anaesthesia, and in this case the anuria is transient and passes off when the blood pressure is restored to normal.

(2) *Renal anuria* is due to destructive changes in the secretory epithelium of the kidney. It occurs in most typical form in acute nephritis, in poisoning by phosphorus or by corrosive sublimate, which cause necrosis of the kidney, or in eclampsia and acute yellow atrophy of the liver.

A somewhat similar form of anuria may occur from the precipitation of sulphonamide drugs if the urine is unduly concentrated, it is deposited in crystalline form in the renal tubules or the ureters.



FIG. 281. Multiple renal calculi composed of uric acid and urates. The stones lie in the renal pelvis and the lower calyces and have given rise to an extreme degree of hydronephrosis of the intra renal type. Note that some of the stones are faceted by mutual pressure.

(Department of Surgery, University of Edinburgh.)



Anuria of renal origin may also be associated with acute bacterial infections of the kidneys and in such cases pre-existing disease of the kidneys predisposes to its occurrence. Anuria may also occur reflexly after sudden evacuation of urine from a distended bladder in subjects of chronic enlargement of the prostate. In such cases the anuria is believed to be due to sudden engorgement of the vessels of the kidney. In rare instances anuria may follow upon blood transfusion and is then due to precipitation of hæmatin from hæmoglobin in the renal tubules. Usually the urine has been of high acidity and salt concentration. Overheating of the transfused blood would seem to be an important exciting factor.

(3) *Post renal or obstructive anuria* is the most important variety from the surgical standpoint. The obstruction may be due to calculi, new growths, accidental ligation of the ureter or inflammatory swelling of the mucous membrane of the renal pelvis or of the ureter. For its development the obstruction must be bilateral or as is commonly the case must involve the only functioning kidney. It is thought that in some instances when one kidney is obstructed the opposite kidney ceases to secrete through reflex nervous inhibition (reno renal reflex).

Calculous anuria may occur under many different circumstances which are often determined by the antecedent condition of the kidneys and the ureters. Swift Joly recognizes four main types: (1) obstruction of both kidneys or of both ureters; (2) obstruction of the only functioning kidney; (3) obstruction of one kidney, its fellow being diseased; and (4) obstruction of one kidney, its fellow being apparently healthy. Clinically the first and second types are sometimes indistinguishable.

Simultaneous bilateral obstruction of the kidneys or the ureters is usually due to calculi. The calculi are often small and are generally impacted in the upper part of the ureter. The presence of a large calculus in one kidney and of a small one in the opposite ureter is usually an indication that the small stone has recently migrated and obstructed the ureter.

Obstruction of the only functioning kidney may occur in either of two sets of circumstances: (1) with a congenital absence of one kidney; (2) when one kidney has been previously removed or has been destroyed by diseases such as tuberculosis or pyonephrosis. Obstruction of one kidney with contralateral disease is one of the commonest types of calculous anuria. The unobstructed kidney is usually the seat either of infection or of chronic interstitial nephritis.

Obstruction of one kidney, its fellow being apparently healthy, rarely gives rise to complete anuria. The anuria is usually temporary and is believed to be due to reflex suppression of urine on the healthy side. It is generally believed that fatal anuria follows unilateral obstruction only when the other kidney is diseased.

In calculous anuria when the kidney is exposed at operation it is found to be enlarged, congested and plum-coloured, and the surrounding tissues are oedematous. The renal pelvis may be distended with urine, but sometimes it is almost empty.

EXTROVERSION OF THE BLADDER (*Ectopia Vesicæ*)

In this congenital malformation there is a defect in the lower part of the anterior abdominal wall and in the anterior wall of the bladder, and through the defect the posterior wall of the bladder appears at the surface. The condition is believed to arise from failure of the forward growth of the anterior part of the cloacal membrane.

The defect is oval or rounded and lies in the mid line below the umbilicus. The posterior bladder wall is projected forwards by the pressure of the viscera behind and forms a bulging swelling of deep red colour, separated peripherally from the skin of the abdominal wall by a ring of fibrous tissue. Usually the umbilicus is displaced downwards and it may be involved in the scar tissue and obscured by encrustations.

The ureters ascend from the pelvic floor and open at the surface near the lower rim of the protrusion, and jets of urine may be observed to issue at intervals. The constant leakage of urine at the surface forms the most distressing feature of the condition. Often from infection or from the irritation of clothes or dressings the exposed bladder surface becomes inflamed and it may be raised in œdematous folds and ulcerated. Carcinoma occasionally supervenes, it is usually an adenocarcinoma arising in mucous membrane, the seat of cystitis cystica.

Exstrophy of the bladder is generally associated with other maldevelopments of the parietes and the lower urinary tract. Usually the symphysis pubis is absent, and the pubic bones, which may be several centimetres apart, are united by a thick fibrous band. The wide separation of the pubes sometimes leads to a waddling gait like that associated with congenital dislocation of the hips.

The exstrophy is accompanied by epispadias, and in the male, the sex commonly affected, the penis is drawn up and fixed to the abdominal wall. Often the testes are ectopic and the scrotum may be ill developed. The prostate and vesicles may be absent or atrophic. In the female there may be maldevelopments of the uterus and vagina.

## CONGENITAL OBSTRUCTION AT THE VESICAL OUTLET

## (Congenital Vesical Sphincteric Stenosis)

In this condition, which is confined to boys, there is from birth difficulty in emptying the bladder. There is difficulty in starting the act of micturition and the stream lacks force and volume, and frequency of micturition and dribbling are usually present.

In the early stages the bladder is small and thick-walled from hypertrophy of its muscular coat, but at a later stage it becomes dilated so as to form an obvious swelling in the abdomen. The neck of the bladder and the upper part of the prostatic urethra are dilated to form a funnel-like prolongation from the base of the bladder, and in many instances a fold of mucous membrane projects into the lumen of the urethra from the region of the verumontanum, or less commonly from the anterior margin of the neck of the bladder.

It is characteristic of this form of urinary obstruction that no difficulty is usually experienced in passing an instrument into the bladder.

If the disease is not treated the ureters dilate and hydronephrosis develops. The ureters may be so greatly dilated as to be felt through the abdominal wall. The ureteral dilatation depends upon a loss of normal valvular action at the uretero-vesical orifice, and this can be readily demonstrated in radiograms after filling the bladder with an opaque fluid when it is noted that the fluid regurgitates into the ureters which appear as tortuous channels with a lumen that may be as great as that of the small intestine. Death usually occurs before the age of ten years from uremia often accelerated by extension of infection from the bladder.

The aetiology of this form of urinary obstruction is not finally settled. Hugh Young attributed the obstruction to the valve-like action of folds of mucous membrane in the prostatic urethra, and he claims to be able to demonstrate such folds by cystoscopic examination. In his experience destruction of the folds is sufficient to relieve the obstruction. Other observers have not been able to demonstrate obstructing valvular folds with such constancy. Certainly at post mortem examination in a number of cases no mechanical obstruction has been found, and their absence has led to the belief that the obstruction is, in some cases at least, of a functional character and due to an inherent defect of the neuro-muscular mechanism concerned in micturition.

### DISEASES OF THE URACHUS

The urachus or allantoic canal develops with the bladder from the ventral part of the cloaca and is about 5 to 6 cm. in length. In embryonic life it forms a patent channel extending from the apex of the bladder into the umbilical canal. In later life it is united with the obliterated umbilical arteries to form the ligamentum commune which extends to the umbilicus. Below it passes into the muscular coats of the bladder. Normally the urachus has a fine lumen which, in about 30 per cent. of subjects, is continuous for a short distance with that of the bladder.

**Developmental Abnormalities.** These are extremely rare and unimportant. In some instances the urachus does not develop, and then the apex of the bladder is found at the umbilicus, where it may form an external fistula. Varying degrees of non-descent of the bladder and consequent imperfect development of the urachus may occur, and they may be associated with retarded closure of the bladder and with external fistulae.

**Cysts and Tumours of the Urachus.** Small sacculations may occur in the lower part of the urachus, they are due to distension by secretion of the normal epithelium-lined spaces. In some instances a urachal cyst is due to degeneration of a small adenoma of the epithelium of the urachus.

*Simple tumours* such as adenoma, fibro-adenoma and fibro-myxoma

have been described but they are exceptionally rare. A sarcoma may arise from the fibrous investments of the urachus, but it also is rare.

A carcinoma may arise from the epithelial remains. It takes origin at the apex of the bladder, which may be invaded by it, but it tends to spread widely in the extraperitoneal tissues before the bladder is extensively involved. A carcinoma of urachal origin is usually of columnar cell type, and often shows colloid degeneration.

## DIVERTICULA OF THE BLADDER

A diverticulum of the bladder may be congenital, but the majority develop in adult life, especially in men over fifty years. They may be single or multiple, and they may be of small size or larger than the bladder itself. Diverticula should be distinguished from the shallow pouches found between the trabeculae of a hypertrophied bladder, from the prolongations of part of the bladder into inguinal or femoral herniae, and from septic paravesical cavities.

**Ætiology.** Diverticula in infants and young subjects are very rare, are usually congenital, and associated with a contracted urethral orifice or valves. In the majority of cases diverticula are acquired in adult life as a result of urethral obstruction, and the extreme rarity of diverticula in women is probably accounted for by the infrequency with which they suffer from interference with the outflow of urine.

Chronic enlargement of the prostate and stricture of the urethra are the two diseases most often responsible for diverticula, and as diverticula are only present in a limited number of cases, it appears that there must be an inherent weakness of the walls of the bladder in some subjects. The prostatic enlargement is seldom more than slight.

Diverticula usually arise just above and lateral to a ureteric orifice at the junction of the trigone with the rest of the bladder, and this rather constant site of origin suggests that in these positions the walls of the bladder are less resistant to pressure than elsewhere.

In rare instances a diverticulum may result from traction caused by adhesion of the bladder to neighbouring organs, and in such cases there may be a history of previous pelvic cellulitis.

**Morbid Anatomy.** Diverticula may be present at any part of the bladder, but they are found most frequently on the lateral walls in the neighbourhood of the ureteral orifice. Less often they are found at the posterior surface of the bladder immediately above the interureteric bar. In many cases the diverticula are placed symmetrically. When they are multiple one of them is often large, the others small.

The orifice of the diverticulum is usually small, with sharply defined margins giving it a punched out appearance when viewed at cystoscopy. An oval or slit like orifice is sometimes found, but it is less common. The ureter may open on the margin of the orifice of the diverticulum, or it may be dragged into the interior of the sac.

The mucous membrane around the orifice is often puckered in a radiate fashion. Trabeculation of the bladder confined to the region of the orifice is often noted, and the interureteric bar may be hypertrophied on the side of the diverticulum.

The diverticulum varies in thickness and all the coats of the bladder are represented in it. The mucous membrane and the submucosa are thin. Muscle fibres are most abundant at the neck of the diverticulum, and if the sac is large they may be attenuated or absent towards its fundus. Its abdominal surface is covered by the perivesical fascia and there is often a considerable deposition of fat around it. From infection it may become adherent to the pelvic viscera.

**Pathological Effects and Complications of Diverticula.** By pressure or by traction a diverticulum may cause constriction of the lower end of the ureter and subsequent dilatation of the kidney, and if infection is present in the bladder ascending pyelonephritis may supervene.

A large diverticulum has no power of muscular contraction and depends mainly on gravity for expulsion of its contents. Stagnation of the urine within it predisposes to infection and therefore cystitis is one of the commonest complications. From the diverticulum stagnant purulent urine may escape from time to time and as a result of infection multiple phosphatic calculi frequently develop. Perforation of an infected diverticulum is a rare complication. A carcinoma may develop at the orifice of a diverticulum or in its interior.

## CYSTITIS

The bladder is remarkably resistant to infection by pyogenic organisms and may remain healthy even though the urine be heavily infected. This is especially true if the bladder is normal in other respects and cystitis is almost always dependent upon some predisposing factor which favours the lodgment or growth of micro-organisms.

The most important predisposing factor is obstruction to the outflow of urine which leads to imperfect emptying of the bladder. For this reason cystitis is common in association with prostatic enlargement or with urethral stricture and it is an almost inevitable complication of lesions of the brain and spinal cord associated with retention of urine. Cystitis is very apt to develop also as a result of urinary stasis in a diverticulum of the bladder or in females as a complication of cystocele.

A second predisposing factor of some importance is the presence of a foreign body in the bladder. A stone for example, frequently determines the onset of cystitis or it may aggravate existing infection. Foreign bodies introduced along the urethra for example lead pencils portions of rubber catheters etc. may give rise to especially severe types of cystitis and even small foreign bodies such as surgical sutures inserted into the bladder wall may aggravate an infection.

Tumours of the bladder also predispose to cystitis probably because they afford an ulcerated surface and an abundance of necrotic material. Malignant tumours are almost invariably accompanied by cystitis and simple tumours are very apt to become infected after fulguration when a part or the whole of the tumour is necrotic.

**The Organisms.** The organisms of cystitis are varied. Coliform bacilli are undoubtedly the most common, especially in the milder forms of chronic cystitis. Staphylococci and streptococci are often present

either alone or with *bacillus coli*. They are especially common in purulent cystitis associated with obstruction to the outflow of urine, and since they render the urine alkaline they are important factors in the production of phosphatic incrustations or stones. Less often, *bacillus proteus*, *bacillus typhosus*, and other organisms are found.

**Avenues of Infection** The avenues of infection in cystitis are not always obvious, and no doubt they vary in different cases. Often it seems likely that cystitis is secondary to an infection of the kidney, for example, pyelitis or pyelonephritis, although it is remarkable, as has already been noted, that in many cases the bladder may withstand such an infection during a long period.

In other cases the bladder is infected by way of the urethra. This is probably the commonest mode of infection, and it seems likely that the comparative frequency of cystitis in the female is due to the shortness of the urethra. In some cases, especially in males, the infection is introduced by a catheter. In normal circumstances the urethra contains few or no organisms, and instrumentation is comparatively free from risk, but when the urethra is diseased or is the seat of stricture even the most scrupulous care will not always prevent the onset of cystitis, especially if the urine is subsequently allowed to stagnate in the bladder.

**Pathological Changes** It is customary to describe two varieties, acute and chronic cystitis, and either may vary considerably in the degree of its pathological changes.

In *acute cystitis* the inflammation affects the whole extent of the mucous membrane, but is especially obvious at the trigone and base of the bladder. The mucous membrane, normally of pale yellowish colour, becomes intensely hyperæmic and of bright red colour. The blood vessels, normally visible as delicate branching filaments, become dilated and tortuous, and there may be petechial hæmorrhages. Flakes of exudate float in the urine and adhere to the inflamed bladder wall.

In some cases of catarrhal cystitis these are the only pathological changes, but often, in addition, the mucous membrane is greatly œdematous and in places eroded, so that the urine contains blood as well as pus and organisms. Rarely, extensive areas of mucous membrane may desquamate.

In *chronic cystitis* the pathological changes vary greatly. They are always most obvious at the base and neck of the bladder, and it is important to observe that in contrast to tuberculous cystitis the regions of the ureteral orifices are not disproportionately affected though they may share in the inflammatory changes.

In the mildest forms of chronic cystitis there may be little change visible except a slight increase in the vascularity of the bladder base, or the bladder wall may appear paler than usual and of yellowish white colour. In other cases the mucous membrane is œdematous, thickened, and with a rough velvety or granular appearance. Sometimes the œdema is considerable, and the mucous membrane is then swollen and projects in smooth, rounded bullæ which may even resemble simple polypoidal tumours. In more severe degrees of cystitis the mucous membrane is ulcerated, and covered with adherent flakes of pus. Ulcerative cystitis is often due to ammonia forming organisms.

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which render the urine alkaline, and often it is associated with the deposition of calcium phosphate, either as incrustations of the ulcerated wall or as calculi

### Rare Forms of Cystitis

**Alkaline Incrusted Cystitis** This form of cystitis is due to the implantation of *B. proteus* in a bladder already the seat of inflammation. It is a very chronic and intractable form of cystitis. The disease occurs most often after childbirth, when injury to the bladder has necessitated catheterization. It may follow operations for enlargement of the prostate or for urethral stricture.

The bladder is generally reduced in size and bleeds readily on examination. The mucous membrane is oedematous, and adherent to it are flat circumscribed plaques of gritty, phosphatic material. The incrustations are usually confined to the trigone and neck of the bladder, but sometimes the whole of the mucous membrane may be affected. When the incrustations are detached a bleeding surface composed of granulation tissue is exposed. The urine is alkaline in reaction and contains blood, mucus and leucocytes. Sometimes gritty material is passed in the urine.

**Cystitis Emphysematosa** This form of cystitis, which may occur in either sex, is characterized by the presence of multiple small gas-containing cysts in the subepithelial tissues of the bladder. The cysts, which are rarely larger than a large pin's head, project towards the interior of the bladder. The whole surface of the bladder may be affected or the lesion may be confined to one zone. The urine may be normal but is usually infected.

**Cystitis Cystica** In this somewhat rare condition, which is found in association with infections of the urinary tract, the mucous membrane of the bladder is the seat of numerous small cysts which microscopically have an adenomatous appearance. The lesion may be confined to the bladder, but very occasionally a similar condition is present in the ureters and the renal pelvis.

The cause of the cyst formation is not certain. Virchow suggested the cysts were due to blocking of crypts of glands in the mucous membrane. More recently it is suggested that cellular degeneration in inflamed and oedematous mucous membrane is responsible. Appearances similar to cystitis cystica have been produced experimentally in rabbits by injuring the mucous membrane of the bladder by curettage.

The cyst formation is usually confined to the trigone and the region of the ureteral orifices. One or more of the cysts may become pedunculated. When several are clustered together they have the appearance of bullous oedema.

**Leukoplakia of the Bladder** In this condition the transitional mucous membrane of the bladder undergoes metaplasia and assumes the characteristic features of a squamous-cell membrane. A similar change has been observed in the mucous membranes of the renal pelvis and of the gall bladder. In the bladder leukoplakia is invariably accompanied by the signs of chronic cystitis, and it is to be regarded as a hyperplastic reaction of the tissues to the irritation induced by

chronic inflammation. Its main pathological significance is that it is possibly to be regarded as a precancerous condition.

**Abacterial Pyuria.** The disease to which this name is applied is characterized by catarrhal inflammation of the posterior urethra and bladder base with pus in the urine but no demonstrable organisms. It always affects men and usually follows coitus. It has been attributed to a virus infection though clear evidence is lacking. The response to arsenicals suggests that a non-syphilitic spirochete may be responsible.

This condition may be related to Reiter's syndrome in which a non-specific urethritis is associated with arthritis and sometimes conjunctivitis.

## TUMOURS OF THE BLADDER

The bladder especially in the male is a fairly common site for tumours. They are generally of an epithelial nature although various types of connective tissue tumour such as fibroma, myoma and angioma have been described.

The majority of bladder tumours take origin in a previously healthy mucous surface but occasionally there are definite precancerous factors. It is well known that aniline dye workers are specially prone to the formation of papilloma and this is attributed to irritation of the mucous membrane by long-continued excretion of the dyes. Scistosomiasis in Egypt frequently predisposes to papilloma and carcinoma. Leukoplakia of the bladder usually associated with chronic cystitis may also be the starting point of a new growth but generally cystitis cannot be regarded as a definite or common precancerous condition.

### PAPILLOMA

#### (Villous Papilloma)

A papilloma of the bladder may be sessile but is usually pediculated. It is much commoner in men than in women and often it arises in early adult life. It may be single or multiple and varies greatly in size, sometimes attaining the dimensions of a golf ball. It shows a special predilection for the base of the bladder at or about the ureteral orifice.



FIG 284. Villous papilloma of the bladder.  $\times 110$ . The villi are seen consisting of transitional epithelium mounted on delicate cores of connective tissue. Note the numerous large capillary blood vessels.

(Laboratory of Royal College of Physicians of Edinburgh)

In its usual form the tumour is pedunculated, and consists of

a central stem surrounded by delicate branching filaments or villi, which give an appearance likened to a sea anemone. In other cases there is no central stem and the villi take origin directly from the mucous membrane of the bladder. Sometimes the tumour is sessile and lobulated, resembling a raspberry.



FIG 285. Villous papilloma of the bladder  $\times 275$ .  
From the same section as Fig 244. Note the elongated type of transitional epithelial cells and the large capillary blood vessels.

(Laboratory of Royal College of Physicians of Edinburgh)

Microscopically, the central core is composed of fibrous tissue which is prolonged in delicate strands into the villi of the tumour. Occasionally the stroma contains plain muscle fibres and elastic tissue. The epithelium, which covers the fibrous core and each

of the villi resembles that of the bladder and is of transitional character. It is composed of cylindrical cells arranged regularly in a radiate fashion. The stroma contains numerous large thin-walled capillary vessels. The great vascularity of the tumour is very apt to cause haematuria, which is often profuse and generally painless. A pedunculated papilloma may become engaged in the urethra and thus cause stricture or retention of urine. Portions of the tumour may be passed in the urine.

At its inception a papilloma is generally a benign growth but is very prone to malignant change especially in elderly persons. Malignant change is evidenced by a more sessile form of growth and by a tendency to involve the vesical mucosa around the pedicle. In some cases the mucosa for a considerable distance around becomes congested and of granular appearance as a result of early neoplastic changes in it. Vesical papilloma is often associated with a tendency to recurrence after operation. The 'seedling' tumours may reproduce the structure of the parent growth or they may assume malignant characters. They may be large and pedunculated but more often are small, multiple and sessile. This form of metastasis is usually attributed to implantation of free cells from the tumour on to the healthy mucous membrane.

## CARCINOMA

Carcinoma of the bladder may originate in a villous papilloma, or it may arise *de novo* in a bladder that has appeared healthy. Usually it

is situated at the base of the bladder, and it rarely originates at the fundus. Two principal varieties of carcinoma are recognized, the papillary and the infiltrating but the appearance and microscopic features vary both in different tumours and in different parts of the same tumour, and between the two principal varieties there are intermediate forms which render exact classification difficult. A third variety, an adenocarcinoma is rare.

The papillary carcinoma generally arises in a villous papilloma. When a simple papilloma undergoes malignant change it grows more rapidly and forms a bulky, soft mass which may eventually fill the greater part of the bladder. Microscopically, the papillary formation of the



FIG. 286 Papillary carcinoma of the bladder  
(Museum of Royal College of Surgeons of Edinburgh)

growth persists but the uniformity of structure so characteristic of the simple papilloma is lost. The epithelial cells are arranged irregularly, and in places are heaped in solid masses. The cells vary in size and shape, their nuclei are hyperchromatic, and mitotic figures are present.

Through impairment of blood supply the central and superficial portions of the tumour are liable to necrosis and ulceration. The ulcerated surface bleeds readily, and sometimes profusely, and the blood may be so copious as to clot in the bladder. The presence of necrotic tissue predisposes to infection and cystitis is very likely to develop.

In addition to enlarging superficially the tumour tends to spread deeply and to infiltrate the bladder wall. The mucous membrane around the tumour becomes thickened and nodular and subsequently

ulcerates. Later fresh tumours may appear in other parts of the bladder. They are especially liable to recur after operative removal of the principal mass.

The infiltrating carcinoma, the so-called epidermoid cancer, may develop in one part of a papillary growth or it may arise primarily. It is generally a scirrhous growth which does not project far into the cavity but spreads widely in the bladder wall. It forms a shallow ulcer surrounded by a raised, indurated margin. On microscopic examination the growth is composed principally of solid masses of epithelial cells supported in a fibrous stroma. Generally in some parts of the tumour there is evidence of papillary formation. Sometimes the appearance suggests a squamous-cell carcinoma, and there may even be cell nests. Tumours presenting this feature are generally presumed to have arisen in mucous membrane that has assumed a squamous-cell type following leukoplakia. Usually they are accompanied by purulent cystitis, and the malignant ulcer may be partly obscured by phosphatic deposits and pus.

Adenocarcinoma of the bladder is rare and is believed to arise in the small tubular glands occasionally found in the mucous membrane at the trigone of the bladder or in an area of cystitis cystica. Tumours of this type tend to project into the cavity of the bladder and to form soft bulky growths, which are very liable to myxomatous change and to necrosis and occasionally distant metastasis.

**Spread of Vesical Carcinoma.** Carcinoma of the bladder grows slowly and spreads principally by direct infiltration of adjacent tissues. At first, and for a considerable time, it remains limited to the bladder wall and at this stage complete extirpation would be possible but for the technical difficulties of the operation and the dangers consequent on diversion of the urinary outflow. Later the tumour infiltrates the soft tissues of the pelvis, and at this stage it is very apt to involve one or both ureters and to cause obstructive anuria, or it may perforate the vagina or the rectum and lead to a urinary fistula. Eventually the tumour may spread to the regional lymph glands. Rarely it metastasizes to distant sites especially to the vertebræ and pelvic bones and to the lungs.

## SARCOMA OF THE BLADDER

Sarcoma of the bladder is a rare tumour which may arise in childhood or in adult life. It originates in the submucous coat of the bladder and grows to large size, forming a soft mass which is very liable to hemorrhage and necrosis. The tumour projects into and may almost fill the bladder, and it spreads also in the connective tissue planes of the pelvis and exerts pressure upon the urethra or the rectum. On microscopic examination it consists principally of spindle-shaped cells. Often in certain parts of the tumour there is evidence of abortive attempts at glandular formation, and there may be areas of myxomatous tissue and even striped muscle fibres. In such cases the growth may be regarded as a mixed tumour or rhabdomyosarcoma.

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## CHAPTER XXXIII

### DISEASES OF THE MALE GENERATIVE ORGANS

**Development of the Genital Tract.** The genital gland (testicle or ovary) first appears as an elongated mass on the medial aspect of the mesonephros or Wolffian body (*see p 609*), where it forms a subsidiary ridge projecting forwards into the body cavity. Lateral to it there appears the Mullerian duct, and both the Mullerian duct and the Wolffian duct partake in the evolution of the genital tract, the Mullerian duct in the female and the Wolffian duct in the male.

At about the seventh week of intra uterine life the genital tract passes through a complex metamorphosis, for at this time the genital gland descends from its primitive position in the lumbar region towards the groin and scrotum, or towards the true pelvis, and with the gland migrate also the upper (cephalad) portions of the Wolffian and Mullerian ducts whilst their caudad ends remain related to the cloaca.

The later changes in these structures vary according to the sex.

*In the male* the Wolffian duct persists in its entirety, ultimately forming the whole length of the excretory (seminal) channel, from the ductuli efferentes of the testis through the tubules of the epididymis, the ductus deferens, and the seminal vesicle to the ejaculatory duct. In addition it forms the prostatic portion of the urethra and the trigone of the bladder, and the ureter and collecting tubules of the kidney (*see p 609*). The greater part of the mesonephros disappears, but traces persist and form the paradidymis (organ of Gervais), a small collection of tubules above the head of the epididymis. The Mullerian duct atrophies almost completely, and only a vestige remains as the minute prostatic utricle.

While the testis and Wolffian duct are migrating towards the groin the ureter and kidney are ascending from the pelvis, and thus the two channels, the ureter and ductus deferens, come to be hooked round each other at the base of the bladder.

*In the female* the Mullerian duct persists, and the cephalad portion forms the uterine tube whilst the caudad portion unites with its fellow to form the uterus, and possibly part of the vagina. The Wolffian duct atrophies (except those parts which form the ureter and the base of the bladder), but traces of it persist. Its upper portion remains in vestigial form as the epoophoron, and its hindmost end is recognizable as a small sinus opening close to the hymen (Gartner's duct). Rudiments of the Wolffian body persist in the broad ligament as the parovarium.

**Anomalies of the Mesonephros.** Abnormal persistence of mesonephric structures may lead to the development of tumours, cysts or fistulae later in life. The commonest are cysts arising in the broad

ligaments from either the epoophoron or the parovarium (*see p. 710*). The Wolffian body is regarded also as the origin of certain retroperitoneal cysts and possibly of mixed tumours (adenosarcoma) in the kidney.

In a few reported cases the Wolffian duct in the female has failed to atrophy, and has persisted as a tortuous dilated retroperitoneal tract, which may extend from the lumbar region to near the hymen discharging a puriform exudate there. In exceptional cases in males the Mullerian duct may form a similar channel.

## TUBERCULOSIS OF THE MALE GENITAL TRACT

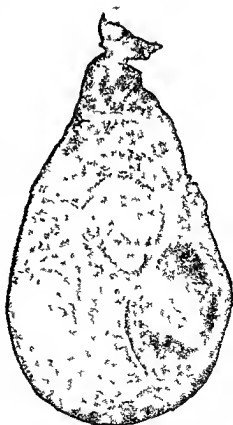
Tuberculosis in the male genital tract commonly involves the epididymis and the seminal vesicles of one or both sides.

It is well known that tuberculous infection of the genital tract frequently complicates renal tuberculosis, and conversely infection of the genital tract often precedes a renal infection.

Much discussion has surrounded the avenue of infection and route of spread of genital tuberculosis. On the one hand, it has been claimed that the seminal vesicle is involved primarily, either by blood borne organisms or as a result of lymph spread from kidney and bladder, and that the disease then spreads down the vas deferens or in the lymphatics of the spermatic cord to the epididymis. There is a possibility that the prostate may be affected primarily and that later extension occurs to the seminal vesicles and the epididymis. On the other hand, there is the view, which at present is the more amply supported, that the epididymis is the primary site of the disease, being infected by the blood, and that from the epididymis the disease is carried along the vas deferens to the seminal vesicle.

In the majority of cases the epididymis is affected alone but the seminal vesicle may be affected later. Often the epididymis and vesicle of the opposite side become involved subsequently.

**The Epididymis.** In the earliest cases tuberculosis of the



**FIG. 28.** Tuberculosis of the epididymis. The globus major is replaced by a large yellow mass of caseous material. The disease has begun to infiltrate the testis which contains numerous pin head tubercles. There is a small chronic hydrocele with thick fibrous walls.

(Museum of Royal College of Surgeons of Edinburgh.)



epididymis is said to affect the globus minor, but it soon involves the entire organ. In mild cases the disease remains limited to the epididymis, and the follicles are walled in by fibrous tissue. Examination will then reveal the presence of discrete nodules, smooth, rounded and of firm consistency, perhaps half an inch or less in diameter. Such nodules may persist for years, giving rise to no symptoms.

In more severe cases the disease spreads more actively. The epididymis becomes greatly enlarged and cow-shaped, so that the globus major overhangs the upper pole of the testis. The tuberculous follicles coalesce until the whole epididymis is caseous. A cold abscess may then form and spread through the adherent scrotal tissues to the surface where it bursts and forms a sinus. Such a sinus is usually situated on the posterior aspect of the scrotum.

From the epididymis the infection commonly spreads up the spermatic cord, which becomes thickened and nodular.

The testis may escape entirely, but often it is involved extensively. Not infrequently the tunica vaginalis is infected and one form of hydrocele results. Natural healing is usual.

**Seminal Vesicle** The vesicle is commonly involved in tuberculosis of the genital tract. It is enlarged and nodular, infiltrated with tuberculous follicles. Generally the disease takes a chronic form, giving rise to no symptoms, and after the epididymal infection subsides the vesicle heals. Less often a cold abscess forms, and bursts into the rectum. In some cases the disease spreads from the vesicle to the prostate.

## DISEASES OF THE PROSTATE GLAND

Acute prostatitis is usually due to extension of a gonococcal infection of the urethra. It may culminate in abscess formation, and there may be extension to the seminal vesicles and the epididymis. Gonococcal prostatitis may be very intractable and may be responsible for recurring exacerbations of infection in the lower urinary tract, or for infection elsewhere in the body, especially in joints.

An acute abscess of the prostate is sometimes caused by the staphylococcus aureus borne in the blood stream from a lesion elsewhere. The abscess usually burrows into the urethra, but it may extend into the retroprostatic cellular tissue and reach the perineum.

After the age of fifty years (sometimes much earlier) the prostate gland may undergo hyperplastic or degenerative changes, and the effects produced are known collectively as *prostatism*, the outstanding feature of which is interference with emptying of the bladder. The pathological changes in the prostate may be considered under the following headings: (1) simple hypertrophy, (2) prostatic fibrosis, and (3) malignant disease.

Reference to the normal anatomy of the prostate is necessary for proper appreciation of the different ways in which the size, texture and relationship of the gland may be altered in these chronic diseases.

From the point of view of surgical anatomy it is convenient to regard the prostate as a fibro-muscular organ permeated by glandular nodules, situated around the prostatic urethra, and at the neck of the

the bladder, with which its central part is directly continuous. The bulk of it lies behind the urethra, and this part of it is traversed by the ejaculatory ducts. The division of the gland effected by the urethra and ejaculatory ducts enables one to recognize five lobes or segments in the gland. At the sides of the urethra are the *lateral lobes*, in front is the *anterior or commissural lobe*, the triangular wedge of tissue between the urethra and the ejaculatory ducts is the *middle lobe*, and the portion behind the ducts and urethra is the *posterior lobe*.

The prostate is enclosed by a fibro-muscular *capsule* or condensation of its own substance, which sends septa into its interior. The *sheath* of the prostate is the pelvic fascia around it, and is of a firm fibrous texture, and except in front and at the apex, or lower end, it can be readily stripped from the organ. Within the sheath lies the prostatic plexus of veins, which is joined anteriorly by the deep dorsal vein of the penis. The veins lie chiefly in the groove between the bladder and the prostate. The prostatic veins enter the anterior part of the plexus, and therefore hemorrhage is likely to occur if this part of the prostate is injured.

The lymph vessels of the prostate drain into a periprostatic plexus, from which trunks pass to the iliac and hypogastric glands.

The muscular fibres of the trigone of the bladder converge upon the prostatic urethra and are attached at the verumontanum. The anterior longitudinal coat passes into its capsule and the inner circular layer of the bladder becomes condensed upon its upper surface to form the internal vesical sphincter.

It is important to recognize that a normal prostate cannot be enucleated by subcapsular dissection for there is no plane of separation between the capsule and the rest of the substance of the prostate. Total removal of the prostate necessitates separation of the capsule from the sheath and as these are intimately united in front the veins of the prostatic plexus are torn. When an enlarged prostate is enucleated through the bladder, damage to the internal sphincter is inevitable, but an intra urethral enucleation may spare the sphincter.

### Simple Hypertrophy of the Prostate (Chronic Lobular Prostatitis)

This is by far the commonest cause of prostatism. The aetiology of the disease is not fully known. The changes in the prostate are very similar in nature to those found in the breast in chronic mastitis, and in the thyroid in adenomatous goitre. It is now certain that the influences which cause the changes in the prostate are hormone in origin and arise in the testis. Experimentally it has been shown that male mice subjected to frequent skin applications of the ovarian hormone oestrin regularly develop prostate enlargement, with urinary obstruction, dilatation of the bladder and bilateral hydronephrosis. It seems probable that the action of this or similar hormones is responsible for prostatic hypertrophy in man. The likelihood is still further suggested by the finding that daily injections of oestrin into immature male rhesus monkeys over periods of six to twenty eight days lead to prostatic hypertrophy in which the epithelium of the utricle (uterus masculinus)

showed very marked proliferation. The view held at present is that the testis secretes an œstrogenic substance as well as the male hormone proper and that the normal balance between the two may be disturbed late in life so that the œstrogenic element becomes predominant and is responsible for the prostatic overgrowth.

The outstanding change is hyperplasia of the connective tissue stroma and of the glands. The overgrowth of fibrous and plain muscle tissue may be such as to lead to fibromyomatous nodules of variable number and size. In addition the glands usually show hyperplasia and in places may undergo cystic dilatation. Corpora amylacea are found scattered throughout the hyperplastic tissues. The microscopic appearance resembles that of a fibro adenoma, but



FIG. 28. Simple hyperplasia of the prostate. Glandular hyperplasia (redonates  
(Laboratory of Royal College of Physicians of Edinburgh.)

as in chronic mastitis the condition is not a true tumour formation but rather a simple epithelial hyperplasia due to some stimulus associated with physiological involution. In some cases however, the resemblance to tumour formation may be strong especially when the changes are restricted to a few areas of the gland. The ratio of fibrous tissue overgrowth to glandular hyperplasia varies in different cases and the size and appearance of the gland are determined by their relative proportions. These hypertrophic changes in the prostate are commonest in the middle lobe, and may be confined to it but in addition one or both lateral lobes are often affected. As a result the unaffected glandular acini are compressed and condensed along with the interglandular stroma. This compression of the normal glandular tissue is of great importance surgically because it creates a false capsule, out of which the hyperplastic part of the prostate may be readily enucleated.

The degree of enlargement in chronic lobular prostatitis varies considerably. On an average the gland is enlarged to about twice to four times its normal size or even more, but in extreme instances it may reach the size of an orange. The enlargement is generally fairly symmetrical. Usually the gland is uniformly firm in consistency, but the consistence varies within considerable limits. When enlargement is confined to the middle lobe this portion projects into the floor of the bladder as a spherical mass or as a collar surrounding the internal meatus, which, when viewed from the bladder, has an appearance somewhat resembling the cervix uteri. It is important to recognize that enlargement of the middle lobe of the prostate cannot be detected on rectal examination.

As a result of enlargement of the prostate there are several important secondary effects on the urethra, the bladder, and the kidneys and ureters.

**Effects on the Urethra** The prostate enlarges in an upward direction owing to the resistance of the triangular ligament, and as a result the base of the bladder is carried upwards, and the prostatic urethra becomes elongated, so that an instrument requires to be passed for a greater distance than normally before it reaches the bladder. The posterior urethra may be more curved than normally, so that a catheter of special shape may be required to traverse it. When enlargement of the prostate is asymmetrical the urethra may be deflected to one side, or it may be narrowed. Often the prostatic urethra is widened from stretching of the mucous membrane over the enlarged gland.

**Effects on the Bladder.** As a result of obstruction to the outflow of urine from the bladder its walls become hypertrophied, and on its interior the muscle bundles become evident as prominent trabeculae, and diverticulation is common. If obstruction is of long standing the bladder becomes dilated and its walls very thin. Protrusion of the enlarged prostate into the bladder causes the orifice of the urethra to be no longer the lowest part of the bladder, and this may lead to accumulation of residual urine. The stagnation of urine predisposes to



FIG 289 Greatly enlarged middle lobe of prostate projecting into the bladder. The bladder is greatly dilated and bilateral hydro-ureter is present.

(Museum of Royal College of Surgeons of Edinburgh)



FIG. 290 Bladder, ureters and kidneys from a case of prostatic hypertrophy. The bladder is trabeculated and there is a diverticulum on the side. Bilateral hydro-ureter and hydronephrosis are present.

(Museum of Royal College of Surgeons of Edinburgh.)

cystitis, which is a very common complication of long-standing prostatic hypertrophy, its occurrence is often precipitated by catheterization. Phosphatic calculi commonly develop as a result of the cystitis.

In many cases one or more diverticula are present near the base of the bladder.

**Effects on the Kidneys and Ureters** As a result of prolonged distension of the bladder the escape of urine from the ureters is impeded, and they gradually become dilated. The sphincteric action normally exerted at the ureterovesical orifice is lost, and when the bladder becomes over-distended reflux of urine up the ureters occurs. The bilateral hydro-ureter is almost always associated with hydronephrosis, which in neglected cases may attain a large size and very little kidney tissue may persist.



FIG. 291 Kidneys from a case of enlarged prostate showing unilateral hydronephrosis and pyelonephritis.

(Museum of Royal College of Surgeons of Edinburgh.)

Subjects of prostatism frequently suffer from chronic interstitial nephritis, and the effects of this are greatly exaggerated as obstruction to urinary secretion advances. It is not surprising, therefore, that features of chronic uræmia may supervene, sometimes they completely overshadow the local effects of the prostatic disease, and they may even lead to a fatal issue in the absence of pronounced disturbance in lower urinary organs.

Stagnation of urine in the dilated ureters and kidneys predisposes to ascending infection from the bladder, and this usually ends fatally. Sometimes infection occurs by the blood stream and leads to acute pyelonephritis with multiple small abscesses in the kidney.

### Prostatic Fibrosis - Chronic Interstitial Prostatitis

In this condition the prostate gland is reduced in size and is of tough fibrous consistence, due to overgrowth of the intraglandular stroma.

The cause of the fibrosis and sclerosis is not known, but it is very probable that it is due to the same factors that in later life cause increase of the interstitial tissue of other organs such as the kidney, liver and breast.

Histologically, both the glandular tissue and plain muscle fibres are compressed and atrophied. The gland is also the site of a round cell infiltration.

In contradistinction to chronic lobular prostatitis no false capsule is formed around the gland, and the whole of the prostate is affected. As a result of the close union of the prostate to its investments no line of cleavage is present to facilitate enucleation. If enucleation is attempted it usually results in laceration of the bladder and damage to the urethra. Therefore the treatment of prostatism of this type must be conducted on different lines from that of chronic lobular prostatitis.

In fibrous prostatitis the prostatic urethra is not elongated, in fact, it may be shortened. When the middle lobe of the prostate is especially involved an unyielding fibrous transverse bar results which causes obstruction at the outlet of the bladder. In such cases the prostatic urethra becomes shortened so that the neck of the bladder and the verumontanum are approximated. If a cystoscope is passed, obstruction is encountered at the entrance to the bladder. On inspection a transverse ridge or ledge is often noted, and the mucous membrane over it is more fixed than normally. Sometimes the fibrous bar instead of projecting as a transverse ridge presents as a firm nodule on the floor of the bladder at the internal meatus. The changes in the bladder are similar to those in prostatic hypertrophy, and are the outcome of interference with the function of the internal sphincter.

*Prostatic calculi* may occur, though rarely. There may be a single calculus, but more often they are multiple, and there may be a large number. They lie within cavities in the substance of the prostate, chiefly in the lateral lobes. They occur most commonly in elderly men, but have been observed in men as young as thirty years. The calculi usually have a nucleus of epithelial debris, blood clot or bacteria, and a shell composed of mixed phosphates and the phosphates, carbo-

nates and oxalates of calcium. They are believed to arise most commonly as a result of long standing low grade infection of the prostate.

In old age there may be extensive calcification in relation to the corpora amylacea of the prostate gland.

### Carcinoma of the Prostate

Carcinoma of the prostate may begin in an apparently healthy gland or in one which is already the site of chronic hypertrophy. It has been estimated that about 10% of prostates removed for hypertrophy show evidence of malignant disease on microscopic examination. This is undoubtedly an over estimate. The disease occurs most often between the ages of sixty and seventy years.



FIG. 20. Metastases from carcinoma of the prostate. A very characteristic appearance of the lumbar vertebrae and pelvic girdle when the seat of metastases from carcinoma of the prostate. The osteosclerosis is very pronounced.

In the early stage malignant disease forms multiple opaque nodules of firm texture, which render the gland unduly hard. The rate of growth of the tumour is usually slow. As the disease advances it infiltrates its capsule and sheath as well as the base of the bladder and the seminal vesicles. At a later stage ulceration of the growth occurs and leads to hemorrhage. Spread to the retroperitoneal lymph glands is a common and early feature. Involvement of the glands is found in at least 60% of cases post mortem. Metastasis to bones is of frequent occurrence and may be obvious before urinary obstruction develops.

Histologically, cancer of the prostate often shows a glandular structure, but sometimes there is less differentiation and the cells are arranged in irregular masses.

A type of cancer is sometimes found in the prostate which differs greatly from the above. The growth begins in the posterior lobe of the gland, and remains confined to it. The growth is small, and is of a scirrhous type, and the gland may be only slightly enlarged, but it is extremely hard. It is characteristic of this type of growth that it often gives rise to widespread metastases in the skeleton especially in the skull, vertebrae and iliac bones, and is associated with an increase of blood phosphatase. At autopsy in such cases the primary growth may be so small as to be readily overlooked, and careful microscopic examination may be necessary to demonstrate it. The changes which may occur in the skeleton are described on p 180. Sarcoma occasionally occurs in the prostate, the tumour may remain encapsuled for a considerable period.

## DISEASES OF THE TESTIS

### Torsion of the Testis

Torsion of the testis seldom occurs in an anatomically normal organ. Incomplete descent, with which other structural abnormalities are often associated predisposes to its occurrence. Torsion may occur in children or in adults, but it occurs most often about the time of puberty. *It is more frequent in the right than the left testis.*

The common anatomical errors of development which predispose to torsion are (1) the presence of a patent processus vaginalis in association with incomplete descent, (2) inversion of the testis, (3) the presence of a mesorchium which separates the body of the testis from the epididymis. In many instances the testis lies more horizontally in the scrotum than normally. When a mesorchium is present the epididymis is found to be completely invested by the tunica vaginalis.

The actual cause of the torsion is uncertain, but as it has frequently followed a sudden strain or a blow, it is believed that a violent contraction of the cremasteric muscle may initiate it. It has also been suggested that a severe strain may cause a sudden engorgement of the tortuous veins of the spermatic cord sufficient to induce torsion.

The site of torsion is usually a short distance above the summit of the testis. In a few instances, where the testis and epididymis are widely separated, only the body is involved. In children the



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FIG. 202. Metastases from carcinoma of the prostate. A very characteristic appearance of the lumbar vertebrae and pelvic girdle, when the seat of metastases from carcinoma of the prostate. The osteosclerosis is very pronounced.

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## DISEASES OF THE TESTIS

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The site of torsion is usually a short distance above the summit of the testis. In a few instances where the testis and epididymis are widely separated only the body is involved. In children the

hydatid of the testis, which is relatively large in early life, may undergo torsion alone. The extent of the twist, which occurs suddenly, varies from a half to one and a half turns, and the rapidity of changes in the organ depends on the degree of torsion. The direction of the twist is always from without inwards. Once established, the torsion is usually maintained, but occasionally it becomes undone spontaneously, but it may recur.

The changes in the testis and epididymis are due to strangulation of its blood vessels. At first, probably, only the veins are involved with the production of venous congestion and swelling of the distal parts. When venous obstruction is long maintained thrombosis occurs, and results in hæmorrhagic infarction of the testis. The arteries may be constricted at the onset of torsion or not until later.

When examined at operation the testis and its coverings are swollen and œdematous, and have a blue discoloration from venous engorgement or thrombosis. The tunica vaginalis usually contains a blood stained effusion. In more advanced cases the testis may have the appearance of a ripe plum, and softening from necrosis may be detected. When treatment has been delayed suppuration of the testis may ensue from superadded infection.

Torsion of the testis is usually associated with very great pain and severe shock. The abdominal muscles on the affected side are rigid, and the thigh is drawn upwards. The scrotum is usually reddened, œdematous and tender, and the testis is retracted towards the inguinal canal.

### HYDROCELE

A collection of watery fluid in the tunica vaginalis may be due to disease in the testis or epididymis (secondary hydrocele), or it may arise without obvious cause (primary hydrocele).

*Secondary hydrocele* accompanies acute or chronic inflammation of the testis or epididymis, such as gonorrhœa, tuberculosis or syphilis, and it is sometimes associated with testicular tumours. The fluid varies in character according to the cause, and it is generally small in amount, though sometimes sufficient to mask the enlargement.

*Primary hydrocele* may arise at any time of life. It has been observed in infancy and it is not infrequent in old age, but it is most common during the fifth and sixth decades. The tunica vaginalis becomes distended and assumes a characteristic pyriform shape. Owing to the anatomical disposition of the tunica the testis lies below and behind the hydrocele. When the amount of fluid is great, the testis becomes flattened from pressure and may undergo a certain amount of fibrosis.

The fluid of a hydrocele is straw coloured and of watery consistency, and its amount varies from a few cubic centimetres to a litre. Its high protein content renders it valuable as a bacteriological culture medium.

Loose bodies may occur within a hydrocele, their origin can be traced to fibrinous deposits on the surface of the tunica vaginalis.

The cause of primary hydrocele is not fully understood. The highly albuminous character of the fluid indicates that it is not a mere transudate. In most cases, the epididymis is thickened, oedematous and somewhat congested, whilst in older patients the prostate is often enlarged and the bladder neck inflamed. On the basis of these observations some authorities regard hydrocele as secondary to a low grade infection of the whole genital system.

A *hydrocele of the cord* is a similar condition affecting a persisting portion of the processus vaginalis in the spermatic cord.

A *hydrocele of a hernial sac* is not uncommon in either femoral or inguinal hernia. It is a collection of watery fluid which forms when the orifice of the sac is occluded, and it is generally due to adhesion or impaction of the omental content of an epiplocele at the neck of the sac.

A *hydrocele with persisting processus vaginalis* is a collection of fluid in a sac communicating with the general peritoneal cavity, and it may be due to any form of peritoneal effusion. The misnomer *congenital hydrocele* is

sometimes applied to the condition. Young persons are affected most often for in them the processus is most apt to be patent. In such subjects the cause of the effusion is often tuberculous peritonitis. In older persons the effusion may be an ascitic collection in disease of the heart or kidneys, or it may be due to chylous ascites or malignant disease of the peritoneum.

**Hæmatocele.** Hæmatocele may result from a crushing injury to the testis as in vaulting, jumping etc. Considerable shock attends the injury. The tunica vaginalis is filled with blood which may or may not clot. The surrounding tissues of the scrotum are greatly discoloured from extravasation of blood. If the blood is not evacuated from the

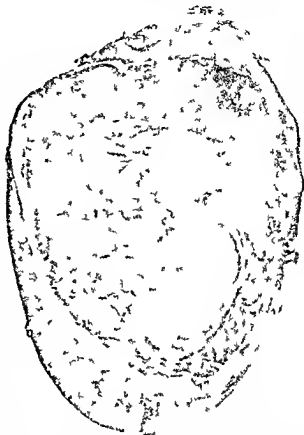


FIG. 23. Hæmatocele, resulting from hæmorrhage into a hydrocele sac. The wall of the sac is rough and discoloured by blood pigment. The testis which has been cut across is compressed and buried in fibrous tissue.

(By courtesy of Sir J. W. Struthers.)

tunica vaginalis organisation occurs and leads to a hard and heavy swelling of the testis

More often the hæmorrhage is attributable usually to a direct blow upon the scrotum or to injury to a vein during aspiration of the hydrocele fluid. Less commonly the hæmorrhage comes from a tumour of the testis or it may be attributable to blood diseases such as hæmophilia, scurvy or severe anæmia.

The effused blood clots and excites an aseptic inflammatory reaction in the wall of the sac. Subsequently young blood vessels invade the clot and eventually its outer layers become organized and fibrous.

In an old standing hæmatocele the wall of the sac is greatly thickened and indurated and it may even become calcified. The inner surface remains rough and shaggy, and discoloured by blood pigment. The testis becomes embedded in the new fibrous tissue and may be almost indistinguishable.

### CYSTS AND TUMOURS OF THE EPIDIDYMISS

Cysts in connexion with the epididymis are common, they may be small and multiple but more often are single.

Multiple cysts are usually situated in the head of the epididymis, less often in the body or the tail. The condition occurs in middle-aged men, and is often bilateral. The cysts vary in size, but they are seldom larger than a pea, they are thin walled, tense and firm, and contain transparent or turbid fluid in which there may be spermatozoa. The origin of the cysts is uncertain: they are said to arise either in remains of the Mullerian duct or from dilatation of the tubules of the epididymis.

Single cysts are more common and may occur in early adult life. The cyst may be unilocular or multilocular and may attain the size of an orange. It is usually situated outside the tunica vaginalis but may be within it and arises either between the globus major and the body of the testis or above the epididymis. As the cyst increases in size it separates the epididymis from the body of the testis, and the vasa efferentia may be stretched over the cyst.

The wall of the cyst is fibrous and often thick, and is lined with columnar or flattened epithelium. The cyst contains opalescent milky fluid of alkaline reaction which on standing separates into two layers: the upper clear and the lower milky, it contains lymphocytes, fat globules, epithelial cells and spermatozoa. In most examples a communication between the cyst and a seminal tubule may be demonstrated. In some cysts the fluid is clear and no spermatozoa are present.

In the majority of instances a cyst of the epididymis arises from rupture of one or more of the vasa efferentia at the lulum of the testes. It is likely that others originate in vestigial remnants similar to cysts of the broad ligament. Thus it is believed that a cyst may arise from the hydatid of the testis (*Morgagni*), *sc.*, from remnants of the Mullerian duct, from the paradidymis (*organ of Giraldès*), *sc.*, remains of the Wolffian body, or from the vasa aberrantia—normal diverticula of the inferior end of the ductus deferens.

Tumours of the epididymis are very rare. Simple tumours, such as lipoma, fibroma, adenoma and leiomyoma, which are the natural outcome of the anatomical structure, have all been encountered. They are seldom larger than a walnut. Sarcoma of either spindle, chondromatous or melanotic type has been observed in a few instances.

A carcinoma may arise from the epithelium lining the tubules. It has been observed most frequently in early adult life, is usually small, irregular and nodular and may be mistaken for chronic inflammatory enlargement of the epididymis. It may extend along the spermatic cord and may involve the coats of the scrotum. The tumour, though usually small, is very malignant, and metastasis to the retroperitoneal glands and the lung is common. Microscopically, epithelial tumours of the epididymis are generally of adenocarcinomatous or rarely of squamous cell pattern.

### SYPHILIS OF THE TESTIS

The epididymis on one or both sides may be enlarged temporarily during the florid stage of syphilis. Enlargement is confined to the *globus major* and is painless and may therefore be unnoticed. Probably the underlying cause is an inflammatory affection of the tubules.

Since the institution of effective methods of treatment of primary syphilis, tertiary lesions, formerly common in the testis, are now seldom observed, but when they occur they almost always involve the body and its investing tunics.

Subjects of inherited syphilis may develop orchitis, which is usually bilateral. It is commonest in infancy or in the second or third year, and syphilis is the only common cause of testicular enlargement in early life. The testis is usually about the size of a pigeon's egg and is hard and painless. The orchitis may be very indolent, but very seldom culminates in gumma formation. When occasion for pathological examination has arisen, it has been noted that the connective tissue between the tubules has been greatly thickened and invaded by lymphocytes and plasma cells.

In adults suffering from acquired syphilis the testis, usually of one side only, may be the seat of chronic enlargement, especially after the second to fourth year following infection. The disease may take the form of diffuse interstitial orchitis or be of a gummatous character.

In the diffuse form there is moderate enlargement of the testis of gradual and painless onset. The testis may retain its normal shape or become spherical. It is hard and woody and is generally devoid of sensation. There is often a moderate sized effusion of serum within the cavity of the tunica vaginalis. Later the tunica vaginalis may be obliterated by adhesions. The tunica albuginea may be the seat of nodular thickening but the epididymis is unaffected. The substance of the gland is infiltrated by newly formed connective tissue disposed radially from the rete testis, and, when cut, the testis retains a flat surface as the tubules are restrained by the fibrous infiltration. Occasionally there is a small central gumma, and less often multiple areas of degeneration. Complete atrophy of the testis may finally occur.

In the gummatous form the appearance of the testis varies according to the stage of the disease and the amount of fibrous infiltration. There may be a single homogeneous yellow necrotic mass in the centre of the greyish red glandular and opaque fibrous tissue which may increase until the entire testis is involved or there may be multiple small areas of degeneration amidst a granulomatous and enlarged testis, such areas usually coalesce and may destroy completely the secretory tubules. From extension of the syphilitic process the scrotal tissues may be infiltrated so that finally the skin and dartos muscle may be involved. Rupture on the skin surface may lead to a typical sloughing syphilitic ulcer or the diseased testis covered by a fungous mass of granulations may project on the surface with the scrotum retracted around it. The testis may herniate to such an extent that scarcely any part of the organ is contained within the integuments of the scrotum.

### TUMOURS OF THE TESTIS

Few subjects in surgical pathology have given rise to such difficulty in classification and interpretation as that of testicular tumours. The difficulty was the outcome of the complex histopathology of these tumours and of the error of drawing conclusions from an examination of only a limited portion of a tumour. Now it is insisted that examination of many parts, preferably by the large section and by special methods of staining is essential if all the components of the tumour are to be classified correctly. Even with these refinements the nature of the tissues may be difficult to define. Careful investigation of large series of cases has helped to dispel some of the confusion that has existed and as a result, the older nomenclature and classifications which were either misleading or cumbersome have been revised and simplified. Two well-defined groups are now recognized (1) The teratoid tumour and (2) the germinal cell tumour (the commonest) known as seminoma usually (spermato cytoma) the first is the common title. Very rarely a teratoma and a seminoma coexist separately in the same testis. There is in addition a very rare type of tumour which originates in the interstitial tissue of the testis—interstitial cell adenoma.

#### General Features of Testicular Tumours

Most tumours of the testis are malignant or potentially malignant and develop in adult life, a few, such as the teratomatous cysts, may be present at birth. In rare instances the disease attacks both testes simultaneously, or the remaining testis may be affected some time later. Malignant disease may attack a retained or ectopic testis and there seems to be good evidence that such maldevelopments increases the liability to malignancy. A history of injury in relation to the occurrence of the tumour is present in almost 20% of instances. The tumour may be very small or may attain large dimensions sometimes rapidly after a long period of latency. The usual site of the tumour (particularly the teratoid variety) is usually the mediastinum of the testis, deep to the tunica albuginea and as growth proceeds the testis

is gradually compressed so that finally it may appear as a wafer at the periphery of the tumour, or it may be incorporated in the tumour. The epididymis remains long unaffected. A small hydrocele or haematocoele may be present, especially after injury.

The urine from subjects of testicular tumour contains gonadotropic hormones which are responsible for the positive Aschheim Zondek reaction. In most the hypophyseal hormone predominates, in a few a chorionic hormone. The hormone output is higher in seminoma than teratoma and greater in embryonal adenocarcinoma and highest in chorionic carcinoma. The test, both qualitatively and quantitatively, may be of some value in diagnosis and prognosis. A seminomatous type of tumour associated with an increased excretion of hypophyseal hormone is radio sensitive and the prognosis is relatively good. In tumours associated with an output of chorionic hormone the prognosis is poor because the tumour is resistant to irradiation.

*Secondary growths from testicular tumours may result from invasion of lymph vessels or of veins.* Lymph borne metastases are usually noted first in the lumbar glands, the inguinal glands are not affected except in the rare event of the tumour having involved the scrotum. Blood borne metastases are common in the lungs and may be present later in other organs. Spontaneous disappearance of metastases is known. In general tumours of the testis have a high degree of malignancy. It has been estimated that survival after ten years occurs in not more than 25% of instances.

### The Teratoid Group of Tumours

A teratoid tumour usually appears between the ages of thirty and forty. It may be smooth or lobulated, soft or hard, at first its growth is limited by the resistance of the tunica albuginea, so that for long the enlarging testis retains its shape. It may give rise to an effusion of clear or gelatinous fluid in the tunica vaginalis, but the effusion is seldom considerable and is not bloodstained unless injury (as from exploratory puncture) has occurred.

On section the testis may be obvious at the summit of the tumour, it may appear normal, but more often it is compressed and appears as a narrow strip of tissue separated from the tumour by a condensed fibrous layer or capsule (see Fig. 294). The tumour may be homogeneous but frequently it shows areas of hæmorrhage or necrosis or cystic spaces containing gelatinous material. Cartilaginous nodules are often present, and may be so abundant that the tumour has the appearance of a chondroma.

Microscopically, the most arresting feature of a teratoid tumour is its complexity. The tissues may be of great variety and may be mature or embryonic, and it may be impossible especially in the case of atypical glandular structures, to specify their character. In some examples differentiation may occur to a remarkable degree and a part of an entire adult organ may be reproduced. But generally the tissues are disposed in a haphazard manner without more than slight attempts at specific associations.



Occasionally one of the component tissues occurs in great profusion and may appear to suppress others. There are, for example, rare tumours of the testis which have the appearance of chondroma, fibroma, adenoma etc., but which can be shown by more thorough examination to be teratoid tumours in which one type of tissue preponderates. The teratomatous cyst and chorionic carcinoma described below are examples of such one-sided growth in these cases the ectodermal elements.

For descriptive purposes it is convenient to catalogue the many tissues which may be found in testicular teratomata according to the germ layer—ectodermal, entodermal, and mesodermal—to which they may be assigned and on this basis the following table indicates the tissues which may be represented.

<i>Ectodermal</i>	<i>Entodermal</i>	<i>Mesodermal</i>
Stratified squamous epithelium with or without keratinisation	Glandular tissue of intestinal type sometimes with mucus secreting cells	All gradations of young fibroblastic tissue
Hair		Myxomatous tissue
Neuro-epithelium which may assume acinar or papillary formations almost indistinguishable from glandular structures	Glandular structures sometimes unspecific but often identical with the thyroid the salivary glands or liver	Fat
Melanin pigmented cells	Ciliated epithelium resembling the bronchial mucous membrane	Lymphoid tissue
Trophoblastic epithelium		Muscle fibres especially plain
		Hyaline cartilage.
		Bone sometimes with hæmopoietic tissues

A testicular teratoma may be composed of a few or a complexity of the above tissues. Superficially they may appear to be disposed in no particular order but none the less there is often a suggestion of correlation of particular tissues. For example it is very noticeable that glandular epithelium especially of intestinal type is often associated with young mesenchymatous tissue in which there may be plain muscle fibres and aggregations of lymphoid tissue. Epithelium like that of the respiratory tract is often found in proximity to bars or nodules of cartilage. Embryonic tissues of the nervous system may occur alongside tissues resembling nerve-sheath elements or a meninx like sheath. In association with squamous epithelium there may be hair follicles, arrectores pilorum, sebaceous material and fat. Probably these specific associations connote an abortive attempt at reproduction of adult structures and are identical with the correlation of tissues which occurs in early development.

Some teratomata of the testis present such characteristic features as to warrant more detailed consideration.

**Tri-dermal Teratoma (Fibrocytic Disease)** This is one of the commonest types. It usually grows slowly, and may appear to be benign. On section its appearance varies according to the relative proportion of cysts, fibrous tissue and cartilage. Areas of softening and degeneration are often present in some part of the tumour. Microscopically, a great variety of tissues may be present but the predominating elements are (a) parts lined by any type of epithelium, stroma which is very cellular, (b) of embryonic type and a variable quantity of hyaline cartilage.

From the pathological side it is important to recognize the great malignancy of the tumour. All the tissues may participate in this activity in different degree, but very commonly the glandular elements show the most active proliferation.

**Teratomatous or Dermoid Cyst** This is the rarest testicular teratoma. It resembles in all respects except size the common ovarian teratomatous cyst (see p 706). The tumour is present at birth, and grows very slowly. Morphologically it represents excessive epiblastic overgrowth in a teratoma.

The tumour is cystic and loculated, is lined with stratified epithelium and contains sebaceous material and hair. Part of the tumour is usually solid and this portion usually contains cartilage, bone, and nerve elements. Malignant transformation seldom occurs in this type of tumour, but it is not unknown.

**Chorionic Carcinoma** This tumour which is probably morphologically identical with chorion epithelioma of the uterus is relatively rare (1%). The tumour is usually small and on that account may be overlooked. It is soft and is very liable to necrosis and hemorrhage and spontaneous retrogression has been observed. Microscopically it is composed of syncytial masses and cells so arranged as to resemble trophoblastic tissue.

The syncytial epithelium has the property of eroding blood vessels, and thus causes extravasation of blood, for the same reason it usually gives rise to metastases in the lungs and later in the liver. The secondary growths appear as hemorrhagic tumours which may become very large.

A chorionic carcinoma may be responsible for breast activity in the male and the pronounced Aschheim Zondek reaction indicates a high prolactin output.

**Malignancy and Metastases in Teratoid Tumours** Teratoid growths according to all standards are extremely malignant and the survival rate is depressingly low. It is important to realize that a teratoma may give rise to metastases and death while the primary tumour is still small but in most cases the features of malignancy are evidenced by fairly rapid increase in size of the testicular swelling.

In the majority of teratomata malignancy is a property of the whole tumour and shared by several or all of its component tissues.



FIG. 34. Teratoma testis with involvement of skin of scrotum and secondary deposits in the inguinal glands. The body of the testis is stretched over the surface of the tumour.

though not always in equal degrees. Formerly malignancy was ascribed to exaggerated growth of one component but this view is erroneous. In the majority metastases occur in the lumbar glands. The gland enlargement may result in a very bulky confluent tumour. Occasionally the supraclavicular glands on the left side are involved probably as a result of invasion of the thoracic duct by cancerous emboli.

Spread by the blood stream is common and is a specially notable feature of chorionic carcinoma.



FIG. 29a. Portion of testicular teratoma, showing skin, hair follicles, sebaceous glands and fat.

(Lancet, by Royal College of Physicians of Edinburgh.)

The structure of the metastases is almost as complex as that of the primary growth; they usually contain two or more of the cellular constituents of the parent tumour. They may show greater differentiation than the primary growth, but usually the reverse obtains. It has been alleged that the metastases may contain tissues not present in the primary growth but this assertion is probably erroneous and based on an insufficiently thorough examination of the primary tumour.

**The Origin of Teratoid Tumours of the Testis.** There are many speculations on this subject and until our knowledge of the origin of teratomata in general is on a more sure foundation dogmatic statements are scarcely permissible. Probably careful examination of very early cases might help to clear up some of the doubts.

Following the theory of Cohnheim that tumours arise from "embryonic rests" it has been suggested without much confirmation that teratoid tumours arise from remnants of the Wolffian body. Others have suggested that they arise from ordinary sex or germinal cells by a process analogous to parthenogenesis and that therefore a teratoma represents a distorted foetus, this theory, though superficially adequate

has not been upheld. Marchand and Bonnet advanced the hypothesis that a testicular teratoma might be derived from an isolated blastomere detached from a segmenting ovum very early in cleavage. This last

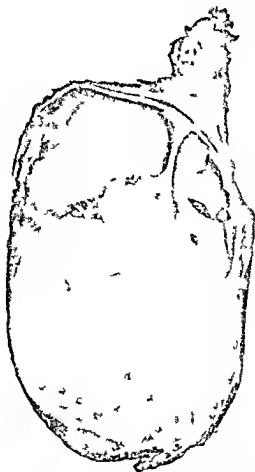


FIG. 996. Seminoma of the testis. Note the convoluted fluid in the tunica vaginalis.

(*Continued from page 672*) University of Edinburgh

view may account for some extragenital teratoma, but it fails to account for their great predilection for the ovary and testis.

As teratoid tumours grow from the region of the rete testis, where developmental errors would be most expected, it is believed that they arise from primitive undifferentiated cells with pluripotent characters that originally arose in the mesothelium of the genital ridge but failed to develop or to become connected with the secretory tubules of the testis.

The exciting cause of the neoplastic development is not definitely known, but trauma appears to play an important part.

#### The Seminoma Group of Tumours

This is the commonest tumour of the testes. It may occur at any period of adult life but is commonest between the ages of twenty and

fo-ty The tumour probably arises from the germinal epithelium of the secretory tubules of the testis, it grows more slowly than

terated tumours and on an average, reaches the size of a closed fist within two years. The tumours (and the metastases) are very radio-sensitive.

In shape the tumour is spherical or ovoid. It is firm and solid, and, except for areas of hæmorrhage or of degeneration which are often present, it is of a homogeneous consistency. The cut surface is fleshy or gelatinous and is intersected by fibrous septa which may produce an appearance of lobulation. The epididymis



FIG. 287. Seminoma of the testis.

*Laboratory of Royal College of Physicians of Edinburgh.*

may be uninvolved, fused to the tumour or indistinguishable.

Microscopically tumours of this class show considerable individual

variation, and even in the same tumour the appearances may not be uniform. In some tumours the cells are large with clear cytoplasm, and resemble the spermatocytes of the testicular tubules; in others the cells are smaller with darkly staining nuclei and much less cytoplasm, while in others the cells resemble lymphocytes. Like the cells of the normal testis the tumour cells are often markedly eosinophilic. The cells are usually arranged in sheets or bands and mitotic figures may be numerous. An embryonal ad-nocarcinomatous type sometimes occurs. A characteristic feature is the presence of small

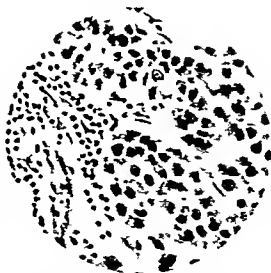


FIG. 288. High power of same section as in Fig. 287.

*(Laboratory of Royal College of Physicians of Edinburgh.)*

A characteristic feature is the presence of small

lymphocytes embedded in small or large groups amongst the epithelial cells. The blood vessels, as in other carcinomata, are often well formed, but in many instances they are thin walled and of embryonic type.

In some examples there is evidence of marked anaplasia and the features of a carcinoma and of a sarcoma are blended—*carcino sarcoma*. Usually the cells are mostly of a carcinomatous character, but, in addition, there are large, round, oval or spindle types, suggestive of sarcoma.

Tumours of the seminoma group metastasize chiefly by the lymph vessels, but occasionally they behave like a sarcoma and give rise to secondary growths in the lungs.

Complete disappearance of metastases has been witnessed following castration.

**Origin of the Seminoma Group of Tumours.** It is generally admitted that these tumours resemble anaplastic carcinoma in other glandular organs and that they are derived from precursor cells of the spermatogonium of the testicular tubules—"embryonal carcinoma". This is borne out by the observation that it is sometimes possible to trace transitions between normal and almost normal seminiferous tubules and frankly malignant tissue, and, in addition, the cells are usually so specific in type that a common origin is the more likely. Nevertheless it must be stated that some observers have attempted to explain the origin of the tumour on the basis of a one sided development in a teratoid tumour.

**Interstitial-cell Tumour.** This is a very rare tumour. It is of adenomatous type and affects the body of the testis. It is small in size and lightly encapsuled and traversed by fine trabeculae which render it lobulated. Its special feature on cross section is its brown colour. Malignant change with metastases has occurred in a few examples. The Aschheim Zondek test may be positive, and features related to an excessive output of oestrogen have been noted. Histologically as would be expected from its origin, it shows disorderly solid masses of polygonal cells in lobular formation. The cells have a granular and particularly acidophilic character.

*The tumour should be regarded as a very rare cause of innocent testicular enlargement.*

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CHAPTER XXXIV

DISEASES OF THE FEMALE GENERATIVE ORGANS

PHYSIOLOGY OF MENSTRUATION

the blood there is a free discharge of mucoid secretion from the glands. At one time it was believed that the greater part of the endometrium was cast, but this view is probably erroneous, and in normal circumstances the loss of tissue is minimal.

(3) *Post menstrual involution* is characterized by retrogressive changes in the endometrium. The blood vessels return to normal size, relief of oedema and congestion allows the membrane to shrink to its former thickness, the effused blood is absorbed and the proliferated cells atrophy and disappear. The glands in collapsing assume a tortuous or plicate arrangement, which in microscopic sections may give a confusing picture, as of acini within acini.

(4) *The interval* is of short duration. During this period the endometrium enjoys a period of relative quiescence, and any physiological loss sustained during the active phases is made good. It is important to note that the endometrium is never in a true resting phase. The phase of repair merges with that of renewed activity, and in microscopic section the features of the two phases are often blended.

**Relation of Menstruation to Ovulation and Reproduction** It has long been recognized that there must be a close relationship between ovulation, the process whereby the mature ovum is discharged from its follicle at the surface of the ovary, and the cycle of menstrual changes, but their correlation in time is not easily determined. Opportunity for observation of the behaviour of healthy ovaries is rarely obtained, and research upon animals is complicated by the circumstance that few animals menstruate, and that the œstrus cycle in animals is not the counterpart of the human menstrual cycle.

It is believed, however, that in women with regular menstrual cycles, ovulation occurs regularly once a month, and it precedes and determines the menstrual flow. The time relationship of menstruation and ovulation has been studied by correlating the menstrual histories of gynaecological patients with the appearance of mature or newly ruptured follicles in the extirpated ovaries, and from these observations it seems probable that ovulation occurs thirteen or fourteen days before the menstrual flow, that is, shortly before the commencement of the phase of premenstrual hypertrophy.

Modern views in regard to the significance of menstruation emphasize the especial importance of the stage of premenstrual hypertrophy. It is believed that this process is designed to prepare the uterus for conception, and that if pregnancy occurs the endometrial hypertrophy passes insensibly into decidua formation. If fertilization is not achieved the hypertrophic state being superfluous comes to an end, and the menstrual flow begins. Thus the menstrual flow is not a preparation for pregnancy but an indication of failure to conceive.

**Ovarian Hormones** The ovary exerts a hormonal control over the whole cycle of menstrual changes, for removal or destruction of the ovaries invariably produces an "artificial menopause."

In recent years it has been demonstrated that there are at least two types of ovarian hormone, derived respectively from the Graafian follicle and the corpus luteum.



Gonococcal endometritis is common, but is never very acute, and is usually obscured by the more obvious effects of gonorrhœa upon the urethra, cervix and uterine tubes. Occasionally acute endometritis follows the use of infected instruments for minor operative procedures. Rarely the infection is blood borne, and it may occur in the course of zymotic diseases, acute tonsillitis, and analogous affections.

### Puerperal Endometritis

The uterus owes its great susceptibility to puerperal infection to the presence of the large placental site composed of spongy decidua without epithelial covering. This forms an ideal nidus for bacteria, and its large blood vessels closed only by recent clot provide a ready avenue by which infection may reach the blood stream.

It was formerly the custom to distinguish two types of this disease, (1) putrid endometritis due to saprophytes, and (2) "septic" endometritis due to bacteria capable of invading living tissues.

It is now generally acknowledged, however, that this classification is somewhat artificial, for saprophytes rarely exist alone, and parasitic organisms may possess any degree of virulence.

In general, two main types may be recognized —

(a) Surface infection of the uterine wall

(b) Deep infection of the uterine wall

(a) *Surface Infection* In the mildest forms of endometritis the effects are those of a localized inflammatory process. The endometrium is covered with soft, dirty sloughs and bathed in foul purulent lochia, and the uterus is enlarged, œdematous, and flabby from toxic paresis. Microscopically, the most striking feature is the great vigour of the reaction. Bacteria and necrotic areas are surrounded by healthy leucocytes, which form dense barriers and effectively prevent invasion of the deeper tissues.

(b) *Deep Infection* In its more severe forms the disease resembles a spreading cellulitis. Sloughs are present on the surface, but the exudate is somewhat thin and often scanty. Microscopically, the organisms are seen penetrating deeply amongst the muscle fibres, which are œdematous and degenerated. Polymorph leucocytes are relatively scanty, and the infection is not circumscribed in any way.

**Complications.** The great danger of puerperal sepsis lies less in toxic absorption from the uterus than in the risk of spread of the infection to other parts.

One of the commonest complications is cellulitis of the connective tissues of the parametrium and broad ligaments. This may arise by direct extension of the disease through the uterine wall, but it is due far more commonly to direct access of the organisms through a laceration of the cervix uteri.

Peritonitis may occur, either by spread of the infection along the tubes or, rarely, as a result of rupture of the uterus during delivery. Peritonitis is generally due to infection with hæmolytic streptococci, and is always of grave import.

risk is greatest of all, moreover, when any form of intervention becomes necessary, especially the manual removal of the placenta

### CHRONIC CERVICAL ENDOMETRITIS (Cervical Erosion)

The cervix uteri is lined on its inner aspect by mucous membrane similar to that of the body of the uterus, but with somewhat taller columnar epithelial cells and more numerous mucous glands. On its outer (vaginal) aspect it is covered by squamous epithelium continuous with that of the vaginal fornices. The mucous membrane of the cervical canal is of deep red colour, the external squamous covering is pale pink, and the junction of the two is situated exactly at the external orifice.

In a cervical erosion the appearance is quite different, for the deep red mucosa transgresses its normal limits and appears on the vaginal aspect of the orifice as an irregularly rounded area the colour of a ripe strawberry. The surface of the area is unbroken (there is no true erosion or ulcer), and it may be smooth or slightly granular. Not infrequently it is studded with small bluish cysts (Naboth's ovules), which result from dilatation of the mucous gland acini. Laterally the 'erosion' merges gradually, in an ill defined line of transition, with the surrounding squamous epithelium.

Microscopically, the surface is usually covered by columnar epithelium, but this may later become replaced in patchy fashion by squamous cells. Deep to the epithelium there are numerous glands like those of the normal cervical endometrium but more complex in structure and more closely set. Collections of lymphocytes and plasma cells are present in the stroma.

Chronic cervical endometritis usually occurs as a sequel to gonorrhœa or to the low grade infection of a laceration of the cervix, but it may develop when there is no evidence of previous disease, and it is not unknown in virgins. On this account it has been suggested that the condition is not infective but is a simple overgrowth of glandular tissue. There is, however, but little support for this view, and there seems little doubt that the condition is a result of chronic infection, aggravated perhaps by the irritative effect of the acid vaginal secretion upon exposed endometrium. Bacteriological examination usually reveals the presence of more than one organism, and this is not surprising in view of the varied bacterial flora of the vagina. Streptococci, hæmolytic or non-hæmolytic, are common, and coliform bacilli, diphtheroids and staphylococci may be present. That elusive organism, the gonococcus, dies out so quickly and is cultivated with such difficulty that it can rarely be demonstrated, but its causative influence may sometimes be suspected.

### CHRONIC CORPOREAL ENDOMETRITIS

Chronic corporeal endometritis may occur as a sequel of definite acute or subacute infections, such as puerperal sepsis or gonorrhœa, or it may occur in women who have had no previous uterine disease, and may even be found in virgins. Two main types may be recognized,

(1) the hypertrophic type, (2) the atrophic type Atrophic endometritis is not uncommon in elderly women, and may then be recognized as a distinct type, the senile type Rarely tuberculous endometritis occurs

(1) **The Hypertrophic Type** In this condition the principal changes occur in the mucosa of the body of the uterus, but the cervical endometrium may be affected to a limited extent On naked eye examination the most striking feature is the great thickness of the mucous membrane, which is soft, velvety and congested Often the whole mucous surface is covered with small raised nodules, and sometimes larger elongated or polypoidal masses project into the lumen

The increased thickness of the mucosa is due principally to great hypertrophy of the glands, which become elongated and very tortuous The epithelial cells proliferate and increase in size and become distended by mucus to goblet shape The acini may be dilated with retained secretion Thus the condition is somewhat similar to that of the physiological proliferation of the premenstrual period Sometimes the glandular proliferation is so extensive as to suggest a neoplastic change, and indeed the condition has sometimes been termed "benign diffuse adenoma" The stroma of the mucous membrane usually presents the signs of chronic inflammation, and is infiltrated by granulation tissue with lymphocytes and plasma cells but in some cases inflammatory cells are scanty or absent and the stroma is fibrous The blood vessels are often thick walled and partially occluded by fibrosis

Hypertrophic endometritis was formerly regarded as the result of infection but the absence of obvious inflammatory change cannot be ignored and the condition is now believed to result from proliferative activity of the endometrium associated with endocrine dysfunction

(2) **The Atrophic Type** This condition is most common after the menopause (senile type), but it may occur at an earlier age It differs from the hypertrophic type in that the endometrium is not thickened by the overgrowth of glands and stroma, but is thin and atrophic The epithelial cells on the surface and those lining the glandular acini become flattened, and many degenerate and disappear, so that eventually on microscopic examination few glands are seen, and such as remain are small and inactive The stroma may contain granulation tissue, lymphocytes and plasma cells, but often there is merely fibrous tissue and no other evidence of inflammation

It has been suggested that often the atrophic type of endometritis is not a bacterial disease but an atrophic process resulting from excessive or abnormal post climacteric involution It is a disease of great importance clinically, for it gives rise to the discharge of blood stained purulent secretion, and may thus be mistaken for a carcinoma of the uterus

### CHRONIC METRITIS (Fibrosis Uteri)

This condition generally shows itself after the age of forty years, and in 90% to 95% of cases affects parous women It is essentially an affection of the fibro muscular wall of the uterus, and the endometrium, though sometimes involved, is not necessarily so

The uterus is enlarged symmetrically, and the consistence of both the body and the neck is firmer than normal. The enlargement is due to the thickness of the wall, which may increase from the normal average of 10 to 15 mm to 25 mm or more. In some cases the increased thickness is due to the presence of an excess of fibrous and elastic tissue, but usually in addition to this there is distinct hypertrophy of the muscle fibres. When the uterus is cut it is seen that the wall is denser and harder than in health. It is little more vascular than normal and may be somewhat pale in colour, but the blood vessels are noticeably prominent on the cut surface, and their lumina tend to gape.

The microscopic appearance differs somewhat in parous and nulliparous women. In either there is extensive muscular hypertrophy and fibrosis, one or other feature often predominating, but in parous women there is also a striking increase of elastic tissue both in and around the blood vessel walls and between the muscle bundles. In either parous or nulliparous women the endometrium sometimes presents the appearance of chronic hypertrophic endometritis.

The cardinal sign of chronic metritis is hæmorrhage, which may be severe and uncontrollable. It is believed generally that the hæmorrhage results from the great proliferation of fibrous and elastic tissue, which prevents the contraction of the blood vessels and the retraction of their bleeding ends, but the alternative view has been proposed that the hæmorrhage is due to associated ovarian dysfunction, of which there is often evidence in the presence of fibrosis and multiple cysts.

The nature of chronic metritis is not clearly understood. In parous women it is usually regarded as a late result of mild puerperal infection or of "subinvolution." Normally in puerperal involution the large uterine arteries are replaced by smaller ones, which penetrate and canalize the organizing blood clot. The wall of the older vessels become fibrous and gradually disappear. It has been suggested that one of the chief factors in chronic metritis is the failure of absorption of the old vessel walls, and particularly of their elastic tissue. The muscular hypertrophy has been regarded as a compensatory process, an attempt on the part of the uterus to control and constrict its bleeding vessels. This cannot account for the process in nullipara, in whom there is no elastic and little fibrous tissue formation. It has been thought that in nulliparae the primary lesion is endometrial, and that the muscular hypertrophy results from physiological efforts to expel the thickened endometrium.

### FIBROMYOMA OF THE UTERUS (Fibroid Tumour)

The uterine fibromyoma is the commonest of all tumours. It is a simple encapsuled growth derived from the fibromuscular tissue of the uterine wall, and it is composed of unstriated muscle bundles and fibrous tissue in various proportions. In small tumours muscle predominates, but increased size and diminished vascularity lead to the development of much fibrous tissue between the bundles. The tumours are generally multiple and numerous, and the uterus may be studded in all parts with nodules of various sizes. In other cases the tumours are

few in number, and one or more of them may reach large size. Occasionally there is a single tumour.

Uterine fibromyoma almost invariably originates during the reproductive period of life, particularly the latter part. It is commonest in childless women, probably because its effects upon the form and vascularity of the uterus prevent implantation of the fertilized ovum.

**Structure.** A uterine fibromyoma is smooth and rounded and completely encapsuled in condensed fibrous tissue. Except when degenerative changes have occurred it is of hard consistency and

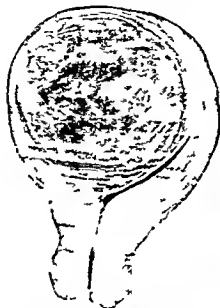


FIG. 299. Interstitial fibromyoma of the uterus. The tumour has undergone red degeneration.

(Department of Midwifery and Gynaecology, University of Edinburgh.)



FIG. 300. Submucous fibromyoma of the uterus. The uterus is distended with blood (haematomata).

(Department of Midwifery and Gynaecology, University of Edinburgh.)

when cut across imparts a creaking sensation to the knife. The cut surface of such a tumour is pale and glistening. The muscle bundles stand out prominently, and their whorled arrangement gives a characteristic appearance as of small tightly packed balls of wool. The periphery of the tumour has usually a plentiful blood supply, but in contrast to this the central portion is often ischaemic. Central degeneration often occurs, and this part of the tumour may be soft and cystic or fibrous or calcified.

Microscopically, the tumour is composed of intertwining bundles of plain muscle fibres separated by various amounts of fibrous tissue. The muscle bundles run in all directions, and in sections some are cut longitudinally, some transversely, some obliquely. The muscle and fibrous tissues are most easily distinguished by van Gieson's stain, for the muscle fibres take up the yellow picric acid and the fibrous tissue

takes up the pink colour of suchism. Apart from their irregular arrangement, the muscle cells resemble those of the normal uterus except that the nuclei are somewhat shorter and more ovoid.

**Varieties of Fibromyoma** The tumour at first lies within the muscular wall of the uterus, but from increase in size and repeated contraction of the surrounding muscle it protrudes in various directions on either the inner or the outer aspect of the uterus.

All are at first *interstitial*, and some remain in this position. Interstitial tumours are commonly multiple and of small or moderate size, but occasionally they are solitary and large. They occur with equal frequency in all parts of the body of the uterus, and occasionally they affect the cervix. Interstitial tumours cause some enlargement of the uterus, often fairly symmetrical. Often they give rise to no symptoms, or they may cause hæmorrhage and dysmenorrhœa.

*Subperitoneal fibromyoma* is almost always multiple. It varies greatly in size, and one or more may attain large dimensions. At first they are sessile, but, with increase in size, they tend to become pedunculated, and eventually may swing freely from a narrow pedicle. The surface of such a tumour is often well supplied with blood vessels, which are evident as dilated channels coursing over it, but the centre is ischæmic. Consequently subperitoneal tumours are usually hard and often calcified, and they are very liable to degenerative changes. Torsion of such a tumour is also apt to occur, especially when the pedicle is long and narrow. Occasionally a large tumour with a short pedicle may involve the whole uterus in its torsion, with serious disturbance of the uterine circulation. Torsion of a fibromyoma leads to various forms of degenerative change and predisposes to infection. Sometimes the tumour becomes adherent to the omentum and viscera, and occasionally such adhesions may be sufficient to maintain the nutrition of the tumour after severance of its uterine attachment (the so-called parasitic myoma).

*Submucous fibromyoma* is less common than the subperitoneal variety and is usually solitary. It protrudes under the endometrium, and as a result of uterine contraction becomes pedunculated, and may eventually project at the external orifice of the uterus. Impairment of the blood supply leads to necrosis and ulceration, often with profuse hæmorrhage.

*Cervical fibromyoma* accounts for less than 5% of all such tumours, a fortunate circumstance, for they sometimes have grave effects. A cervical tumour causes great elongation of the cervical canal, displaces the body of the uterus upwards, and projects forwards towards the bladder, backwards towards the rectum, or laterally into the broad ligaments. In any of these situations it may cause pressure and give rise to grave complications during parturition.

**Degenerative Changes in Fibromyoma** Owing to the paucity of its blood supply, a uterine fibromyoma is liable to degenerative changes, where the vascularity is least adequate. Degenerative changes may occur at any time, but they are most common during pregnancy or at the menopause. Sometimes volvulus of a pedunculated tumour determines the onset.

*Mucoid or Hyaline Degeneration* is the commonest type. It affects the cells of both the muscular and the fibrous elements of the tumour. The cells lose their definition, the fibrillar structure is lost, and a glassy hyaline material makes its appearance. As a result of the degeneration cystic spaces often develop with rough, irregular walls and yellow honey-coloured fluid content. Sometimes the cysts coalesce, and occasionally the greater part of the tumour becomes cystic.

*Ped degeneration or necrobiosis* is a curious type of degeneration believed to result from fairly rapid interruption of the blood supply of a vascular tumour. There is much evidence to suggest that it is due to thrombosis or infarction, and that the peculiar changes are due to fatty degeneration with the liberation of hæmolytic lipid substances. The condition is common during pregnancy since a fibromyoma is then unduly vascular but it may occur at any time.

The central part of the tumour is affected first and to the greatest extent. It becomes softened, and in places almost of fluid consistency. On section it is seen to be of deep red colour like raw meat and it exhales a sickly odour. The red colour is due to hæmoglobin, which is liberated by rapid hæmolysis of extravasated blood cells. Microscopically there is extensive necrosis of the cellular elements, and nuclei are absent or faintly stained. In later stages parts of the tumour liquefy and irregular cystic spaces appear, containing structureless debris and brownish fluid. Much of the affected tissue does not become completely necrotic, and may survive and regenerate, hence the less preferable name *necrobiosis*.

*Fatty degeneration* is very often visible microscopically, either alone or with other degenerative changes, but it is rarely met with to a degree appreciable to the naked eye.

*Calcification* occurs most often in the avascular subserous tumours, especially in elderly women. The calcium deposits may be scattered diffusely through the tumour or may form a thin irregular shell close under the surface. Sometimes the whole tumour may become calcified (the so-called womb-stone) and rarely such a tumour may loosen from its attachment and come to lie free in the peritoneal cavity.

*Infection* is most common in sloughing submucous fibroids. In subserous fibroids it is apt to occur after torsion of the pedicle the organisms presumably being blood borne. Rarely infection by blood borne organisms may arise as a sequel to necrobiosis.

*Malignant Change in Fibromyoma.* It has been said that 1% of fibromyomata eventually become sarcomatous but general experience suggests that this is an unduly high estimate and many authorities agree that malignant change is extremely rare. Sarcomatous change has been observed most commonly in small areas in otherwise simple growths and in these cases the evidence has been based upon microscopic examination.

## ENDOMETRIOMA ADENOMYOMA

An endometrioma, or adenomyoma, is a simple tumour composed of glandular tissue and stroma resembling the uterine mucosa, sometimes

incorporated in masses of plain muscle tissue. Such tumours are observed most often in the uterus but they may arise in the ovary or in other parts of the pelvis lower abdomen or abdominal wall.

An endometrioma occurs only in females, and it arises always during the reproductive period especially after the thirtieth year. It is remarkable in possessing a functional activity which corresponds closely to that of the normal endometrium. It undergoes the same cycle of changes and at the menstrual periods it proliferates, becomes congested, and discharges blood stained fluid. Rarely it may even become the seat of decidua formation. Its pathological features differ somewhat according to their origin.

A uterine endometrioma resembles an ordinary fibromyoma very closely, and in some the distinction can be made only by microscopic examination. The tumour arises most often in the upper part of the body of the uterus, especially on its posterior aspect near the cornu, and it does

not affect the cervix. In some cases it is more or less circumscribed but usually it takes the form of a diffuse thickening of the uterine wall. When cut it presents a dull grey or pink appearance and may be cystic. Under the microscope it is seen to contain tubules or cysts lined by columnar epithelial cells surrounded by a stroma like that of the normal endometrium, the whole embedded in fibrous tissue and a variable amount of plain muscle.

An extra-uterine endometrioma is situated most often in relation to the ovaries or in the uterine tubes or the recto vaginal septum. Occasionally it arises on the intestines at the umbilicus in laparotomy scars or in the round ligaments of the uterus. In any of these situations it is a small tumour composed of glands and stroma of endometrial type often with cysts.

An ovarian endometrioma is usually represented by cysts of hæmorrhagic character often known as tarry or chocolate cysts. Often both ovaries are affected. The cysts are thick walled and usually are densely adherent to surrounding structures. They may rupture into the peritoneal cavity or may form localized fluid collections in the pelvis (see p. 702). Endometrioma in the recto vaginal septum varies in size and may attain the dimension of the foetal head. Usually it is adherent to the vagina and rectum and it may invade these organs.



FIG. 301. Endometrioma of uterus. Acini lined by columnar cells are set in a stroma of fibrous tissue and plain muscle.

(Department of Pathology University of Glasgow.)



*Endometrioma of the intestines* is a small tumour, single or multiple, situated on the peritoneal aspect of the gut, especially on the pelvic colon. It appears as a roughening or granulation, and gives rise to dense adhesions. *Umbilical endometrioma* forms a small tumour which occupies the umbilical depression. At the menstrual period it enlarges visibly, assumes a red or purple colour, and becomes painful. It may become cystic or may open at the surface and discharge a blood stained fluid. *Endometrioma in laparotomy scars* occurs generally after operations for ventral fixation of the uterus, and in appearance and behaviour it resembles the umbilical tumours. *Endometrioma of the round ligament* of the uterus forms a small rounded or oval mass situated either in the inguinal canal or in the groin or labium. It is generally ill-defined and adherent to neighbouring fasciæ, or it may be circumscribed and encapsuled. It may be mistaken for an omental hernia, and often a hernia is present.

**Ætiology.** Many theories have been advanced to account for endometrioma, and none is yet generally acceptable. It seems probable that the uterine and extra uterine tumours differ in their modes of origin.

It is generally agreed that a uterine endometrioma is due to sequestration of endometrium in the wall of the uterus or in a fibromyoma, and that the isolated mucosa causes a reaction of the tissues around it so as to form a tumour. It is believed that the dislocation of endometrium is favoured by chronic endometritis.

The exact origin of extra uterine endometrioma cannot be regarded as settled. At one time it was thought that the tumour was derived from remnants of the Wolffian body or of the Müllerian duct sequestered during development, but such a thesis is inapplicable to endometrioma in such situations as the abdominal wall.

At present there are two principal theories. The first, originally propounded by Iwanoff in 1898, and vigorously supported by Meyer, is based upon the fact that the endometrium, being formed from the Müllerian duct, is derived originally from the primitive coelomic epithelium and is thus closely allied embryologically to the lining cells of the peritoneal cavity. According to this serosa-epithelial theory, endometrioma arises from peritoneal cells that have undergone metaplasia, either as a result of inflammation or in response to excessive secretion of oestrin, the hormone that normally controls endometrial hyperplasia.

The second theory, to which most authorities now adhere, is the implantation theory put forward by Sampson. According to this view, endometrioma arises from adult endometrial cells that have been set free from their uterine bed and implanted in other sites. Harbitz has shown that endometrium transplanted experimentally in rabbits readily takes root in other tissues, and there responds to the influence of ovarian hormones and undergoes the same periodic changes as normal endometrium. It is thought that in some cases, notably in endometrioma in laparotomy scars, the cells are dislocated from the uterus as a result of the operation trauma. In others, the transference of endometrium is believed to be due to a process of retrograde menstruation, whereby endometrial fragments discharged during menstruation are

carried along the uterine tubes and extruded into the peritoneal cavity

## CARCINOMA OF THE UTERUS

This is one of the commonest of all malignant tumours. In England and Wales it is responsible annually for the death of over 4 000 women many in the prime of life. This mortality is only rivalled by that from cancer of the breast and cancer of the stomach.

Carcinoma may arise in the neck or in the body of the uterus and in these situations it differs greatly in its incidence, progress and effects. Carcinoma of the cervix uteri is common, affects women who have borne children, and progresses rapidly. Cancer of the body of the uterus is less common, occurs at a somewhat later age, principally affects nulliparæ and is less malignant.

### Carcinoma of the Cervix Uteri

Over 90% of uterine cancers arise in the cervix. They arise most often during the age period from thirty five to fifty years—the period of functional senescence of the uterus—but are not uncommon a decade earlier. It is a striking fact that fully 96% of cases occur in women who have borne children and there can be little doubt that this incidence depends upon the liability of the cervix uteri to laceration or other damage during childbirth. It is generally stated that women of more than average fertility are especially liable but Deelman and others have shown that when their relative preponderance in the general population is taken into account multiparæ are little more subject to the disease than uniparæ. The trauma of the first labour is the determining factor. It is interesting to note that cancer of the neck of the uterus is rare in Jewesses.

The tumour may arise from the squamous epithelium covering the outer aspect of the cervix, or from the columnar cells of the endometrium lining the cervical canal or its glands. In some cases there is evidence that a cervical erosion provides the starting point.

All tumours of the cervix ulcerate readily and consequently one of the first signs of carcinoma is hæmorrhage which is especially apt to occur after coitus. Infection commonly supervenes and results in a thin sanious discharge often irritating and extremely offensive. In the later stages there is grave toxæmia from septic absorption.



FIG 30. Carcinoma of the cervix uteri. The tumour is of infiltrating type and has destroyed the greater part of the cervix and begun to invade the body of the uterus. The surface of the tumour is extensively ulcerated.

(Department of Midwifery and Gynaecology, University of Edinburgh.)

**Gross Varieties** Carcinoma of the uterine neck, like growths elsewhere exhibit variations both in outward appearance and in behaviour. It is customary to recognize three principal forms which are variations from the average rather than distinct types.

(1) *The Infiltrating Variety* This is the commonest and the most malignant form. It

usually arises at the external orifice of the uterus at the site of an erosion or laceration and spreads both on the vaginal aspect and along the cervical canal. Less often it is entirely within the canal and is then not obvious on vaginal examination. The growth tends to infiltrate surrounding tissues but does not project into the lumen to any great extent. Usually it ulcerates early.



FIG. 303. Carcinoma of the cervix uteri.  $\times 90$ . The tumour is of basal-cell type and is composed of solid alveoli of spheroidal cells which have infiltrated the uterine muscle.

*Laboratory of Royal College of Physicians of Edinburgh.*

lumen and forms a large soft fungating mass which is very prone to bleed. In rare cases it may attain such size as to fill the whole vagina.

(3) *The Atrophic Variety* This is the rarest form and is chiefly met with in older women. It takes the form of a small indurated plaque which may be limited to the vaginal aspect of the cervix. Ulceration occurs early but the growth spreads slowly and is somewhat less malignant than the other forms.

**Microscopical Appearances.** In most cases the growth is a squamous-cell carcinoma, but it differs in several respects from tumours of this class arising in the skin. It is composed of broad solid masses and branching columns of epithelial cells but except in rare cases there are no cell nests and prickly cells are usually absent. On casual inspection the tumour may be taken for a basal cell carcinoma but the cells usually show clear evidence of malignancy as indicated by mitotic figures and aberrations of form and nuclear character.

Degenerative changes in the centres of the epithelial masses lead to irregular spaces which may simulate glandular acini and further confusion may be caused by the almost invariable presence of inflammatory change due to septic infection.

(2) *The Proliferative*

*Variety* This is less common and is generally believed to be less malignant. It grows principally towards the

In a small proportion of cases the growth is a columnar cell adenocarcinoma, and sometimes glandular and squamous elements coexist.

**Extension of the Tumour.** Cancer of the cervix uteri has little tendency to disseminate and its gravity depends upon the tendency to local spread. The malignant cells soon invade the muscular coat, whence it is an easy step to the lymph vessels of the parametrium. Later the bladder, rectum, ureters and the peritoneum may be involved. The body of the uterus is sometimes invaded, but usually to a remarkably small extent.

Lymph glands may be involved early or late. The principal lymph channels follow the uterine artery. Some of them terminate in small glands at the base of the broad ligament while others pass directly to glands along the iliac vessels and in front of the sacrum. Often glandular enlargement found at operation is of inflammatory origin due to superadded septic infection.

Extension of the disease beyond the uterus may cause distressing complications in the later stages. Involvement of pelvic nerves gives rise to severe pain. Invasion of bladder, ureters and rectum may lead to fistulae between these channels and the vagina. More frequently, pressure upon the ureters leads to hydronephrosis and suppurative nephritis and eventually causes suppression of urine. Chronic uræmia is one of the most frequent causes of death.



FIG. 204. Adenocarcinoma of the body of the uterus.  
(Department of Midwifery and Gynecology University of Edinburgh.)

### Cancer of the Body of the Uterus

Less than 10% of uterine cancers affect the corpus uteri, and growths in this situation differ from those at the cervix in both incidence and behaviour. Nulliparae are far more liable to corporeal than to cervical cancer, and are affected in a considerable proportion of cases. The age incidence is somewhat later and the disease is rarely seen before the menopause. This feature aids early recognition for the cardinal sign hæmorrhage is more likely to attract notice after the menopause than at an earlier age. Cancer of the body of the uterus frequently occurs where the organ is the seat of fibromyoma and it is sometimes held that there is a relation between the two conditions.

The tumour arises in the endometrium and forms a mass of soft consistence which projects towards the uterine cavity. Several varieties are described according as the tumour is bulky or ulcerating. The ulcerated form is the less common. Sometimes there are multiple

nodules of carcinoma, which project in polypoidal fashion from different parts of the wall. Occasionally the whole endometrium is affected diffusely.



FIG. 31a. Adenocarcinoma of the corpus uteri.  $\times 250$ . The tumour is composed of columnar cells arranged in irregular acini.

(Courtesy of Lynn C. Cole of Physicians of E.F. Sharp.)

Microscopically, the growth is an adenocarcinoma. It is composed of columnar cells, which for the most part are arranged in acini. Sometimes the acini are few and the cells lie in solid masses—the so-called carcinoma simplex. The acini are usually irregular in size and shape, but sometimes they can hardly be distinguished from the glandular spaces of normal endometrium. In such cases the diagnosis is made upon evidence of invasion of the growing edge, and upon changes in cell form and nuclear structure.

The progress of cancer of the body of the uterus is slow, and thus the prognosis after operative removal is more hopeful than in cancer of the cervix. For a long time the disease may be limited to the uterus itself. Eventually the parametrium is reached, and neighbouring viscera may then be affected. The lymph glands are involved at a late stage.

## SARCOMA OF THE UTERUS

Sarcoma of the uterus is uncommon. It may occur at any time of life, even in infancy, and unlike carcinoma, it is more apt to involve the body than the cervix.

Sarcoma may arise in the fibromuscular wall of the uterus or in the endometrium, and it is usually difficult to determine the exact site of origin.

It is generally stated that sarcoma commonly arises in a fibromyoma but it seems probable that this view is inaccurate and that sarcomatous change in a fibromyoma is exceedingly rare. Sometimes the origin of the tumour may be traced to the plain muscle fibres of the uterus, and the growth may then be regarded as a myo-sarcoma. Rarely striped muscle fibres are present, and the tumour must then be looked upon as a mixed mesoblastic tumour. Whether derived from the fibromuscular wall or the endometrium, a uterine sarcoma may be circumscribed or diffuse.

**Circumscribed Sarcoma** A circumscribed sarcoma forms a soft tumour which grows rapidly. The cut surface is usually brain like of greyish colour, but interrupted in places by areas of necrosis and haemorrhage or by irregular cyst like cavities containing debris and blood clot. Microscopically, there are round and spindle shaped cells and sometimes multinucleated giant cells.

**Diffuse Sarcoma** A diffuse sarcoma appears to originate in the endometrium and it may spread over the greater part or the whole of the inner aspect of the uterus. In such a case the uterus is uniformly enlarged and resembles the pregnant uterus. The endometrium is greatly thickened and its surface shaggy and ulcerated or covered by nodular or polypoidal outgrowths. In some cases the line of separation between the endometrium and the fibromuscular wall is distinct but often both layers are diffusely infiltrated by the tumour. Microscopically spindle cells and round cells are present. Blood vessels are numerous large and thin walled. The epithelial elements of the endometrium are usually destroyed but occasionally a few of the endometrial glands persist.

Two special varieties of uterine sarcoma deserve further mention —

(1) **Recurring Polyp** In a certain proportion of cases recurrence takes place after curettage of submucous uterine polyp and eventually after repeated recurrence true malignant invasive properties may develop. In such cases no doubt the tumour is a submucous fibromyoma that has undergone sarcomatous change and in others the tumour is probably of low grade malignancy.

(2) **Grape-like Sarcoma (Sarcoma Botryoïdes)** This tumour may occur in infancy childhood or adult life. It arises in the cervix and projects towards the vagina where it forms a lobulated mass somewhat resembling a bunch of grapes. Sometimes the tumour attains great size and it may fill and distend the whole vagina. The tumour is composed of round or spindle shaped cells set in a very oedematous matrix which explains its soft, cyst like character.

## TUMOURS OF THE CHORION

The chorion, the outer covering membrane of the embryo is endowed with the property of invading the uterine wall. In virtue of this property it ensures the proper implantation of the ovum and its subsequent nutrition from the maternal blood stream. In normal circumstances this great capacity for proliferation and invasion is restrained and only proceeds to the extent required by the needs of the embryo and at the end of pregnancy the whole zone of invasion is cast off in the placenta. In rare cases however, and in circumstances at present unknown the invasion of the chorion proceeds unrestrained and a tumour results.

It is necessary to consider first the normal structure of the part. The chorion is an embryonic tissue and consists of a stroma of mesoblastic origin and a covering layer the trophoblast derived from ectoderm. The trophoblast is made up of two layers an inner layer of a single row of *Langhans* cells—large well defined cuboidal cells with dark nuclei and clear cytoplasm—and an outer layer the syncytium.

but there seems little doubt that the degenerative changes have an underlying neoplastic basis. Next in the series is the *invasive mole* or *chorioadenoma* (Ewing). This is sometimes classed as a form of hydatid mole, but it differs essentially from this in the extent of invasion of the uterine wall, and, as Novak has pointed out, it is better regarded as a carcinoma of low malignancy. Lastly, there is the *choriocarcinoma* (*chorion epithelioma*), a growth of intensely malignant character.

All the tumours of this class differ in one important respect from most other neoplasms, namely, that they are not derived from the host but from another individual, the embryo. They are parasitic growths, and in this respect they are comparable to certain kinds of teratoma.

**Hydatidiform Mole (Vesicular or Placental Mole)** This condition is generally regarded as a degenerative change affecting the chorion, but there is evidence to suggest that in some cases at least it is more correctly looked upon as a form of abnormal proliferation bordering on neoplasia. It is a rare condition, and is said to occur only once in every two or three thousand pregnancies. Multiparae are affected more often than primigravidae, and sometimes the disease reappears at subsequent pregnancies. The mole starts in the early months of pregnancy, and is rare after the fourth month. When it occurs early and affects the whole placenta the embryo disappears and no traces of it can be found. When the mole occurs later, or when it affects only a part of the placenta the embryo may survive for a short time, but sooner or later abortion occurs. The mole is usually cast off at the time of abortion, but a part of it may remain in the uterus and continue to grow.

The mole is composed of clusters of small, tense lobules which are often likened to white currants or small grapes. Sometimes it may attain a weight of two or three pounds. Haemorrhage occurs readily, and often the mole is partially buried in clots of blood.

Microscopic examination shows that the grape-like structures are distended, hyperplastic villi of the chorion (see Fig 308). The central

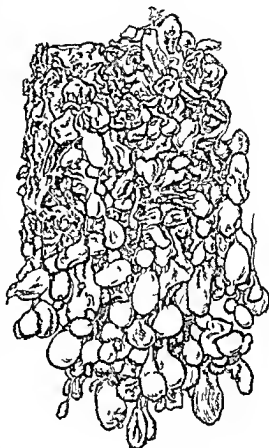


FIG 307 Hydatidiform mole  
(Museum of Royal College of Surgeons of Edinburgh)

The tumour develops in retained portions of a hydatidiform mole but it may occur in an otherwise normal pregnancy or puerperium. Occasionally it has been observed several years after childbirth or abortion. In the great majority of cases it arises in the uterus but occasionally in the vagina, uterine tube, or ovary. Tumours of the structure of choriocarcinoma have occasionally been observed in other situations, for instance in the testis. Such tumours are to be regarded as teratomata, with a preponderance of ectodermal structures.

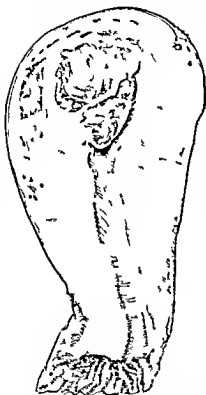


FIG 309 Choriocarcinoma of the uterus. The tumour is situated at the fundus of the uterus. A part of it projects into the uterine cavity while the major part infiltrates the wall adjacent

(Museum of Royal College of Surgeons of Edinburgh)



FIG 310 Choriocarcinoma  $\times 275$ . The tumour is composed of confused masses of chorionic epithelium. The middle part of the figure is occupied by syncytial masses while above and below there are collections of Langhans cells.

(Laboratory of Royal College of Physicians of Edinburgh)

In the uterus the tumour commonly arises at the placental site. The principal mass lies in the muscular wall and projects on the inner aspect of the uterus. Sometimes it extends to the peritoneal surface. It forms a soft friable mass, and owing to hæmorrhage it is of claret or maroon colour. The surface is ulcerated and bleeds freely.

Microscopically, there are islets of actively growing cells of the Langhans type, mingled with irregular masses and strands of syncytium. Blood vessels are particularly susceptible to the invasive properties of the syncytium and therefore extravasations of blood surround and infiltrate the growth. The uterine wall is extensively invaded, and tumour cells may be seen lying in the lumen of the blood sinuses. The



growth possesses no stroma, and has no blood vessels of its own and is nourished from its host

*Choriocarcinoma* progresses rapidly, and death usually takes place within from six to eighteen months. The growth disseminates by the blood stream especially to the lungs. Sometimes secondary growths appear in the vaginal wall and elsewhere in the pelvis. It is often stated that metastases may disappear spontaneously after removal of the primary growth but according to Ewing such behaviour is rare in true choriocarcinoma though not uncommon in syncytioma.

*Syncytioma* In 1895, Marchand who was the first to demonstrate the chorionic origin of chorion epithelioma, distinguished two forms, the typical form (which corresponds to the description of choriocarcinoma above), and the uncommon atypical form. The latter is now generally known as a syncytioma. It is a bulky tumour which infiltrates the uterine wall, but differs from the "typical" form in its great tendency to retrogression. It is composed of large giant cells with the general characters of chorionic syncytium. These are scattered diffusely and mingled with masses of fibrin and necrotic debris in which are numerous wandering and inflammatory cells. The condition is sometimes regarded as a distinct tumour with a definite tendency to retrogression, but according to Ewing it is merely a degenerative form of one of the less malignant types of chorionic tumour.

*Ovarian Changes in Chorionic Tumours* Marchand drew attention to the frequent association of ovarian cysts with chorionic tumours, an observation which has been amply confirmed by subsequent experience. The cysts are of lutein type and may affect both ovaries and be so large that they are palpable above the pubes. Their nature is not known. The hormone *lutein* is believed to control implantation of the ovum and it may also control growth of the chorion, but there is no evidence that abnormal lutein production predisposes to the growth of the tumour. It is known that the corpus luteum itself is controlled by other secretions possibly of placental origin, and the ovarian cysts are probably due to excessive production of this secretion. This would explain the disappearance of the cysts which sometimes follows successful removal of the tumour.

### SALPINGITIS

Salpingitis results usually from infection from the uterus and vagina, less commonly from a contact infection from adjacent structures, such as the appendix, and rarely, apart from tuberculous salpingitis, from haematogenous infection. The majority of cases of acute salpingitis are of gonorrhoeal origin.

Chronic salpingitis, excluding tuberculous disease, is almost always a sequel to an acute or subacute attack. In virtue of the innumerable folds and crevices in its mucous membrane, the tube forms an ideal site for the maintenance of infection especially by organisms of low grade virulence, such as gonococci. Chronic gonococcal salpingitis is therefore common and may be of any grade of severity.

The disease may arise a short time after the primary infection, or after a long interval. If delayed it may depend upon some exacerbation of the disease in the urethra or cervix, or it may represent a recrudescence of an earlier mild infection of the tube. Usually both tubes are affected.

The mucous membrane is principally involved, and its many folds become congested and greatly swollen by oedema. At an early stage the fimbriae are swollen and turgid, and from the abdominal ostium a few drops of yellow pus may be expressed. At this stage there is commonly a mild degree of peritonitis, principally limited to the pelvis. The pelvic peritoneal surfaces are congested and lose their normal sheen, and the cavity contains a small quantity of sero-purulent exudate. In some cases the peritonitis is more extensive. The whole lower abdomen may be affected, and the coils of ileum may be glued together by lymph exudate. A purulent collection may form in the pelvis.

The acute phase almost invariably subsides in the course of a short time, but complete resolution often does not occur. There is a very great tendency to the formation of adhesions, either delicate filmy membranes, or tough bands of fibrous tissue.

In chronic salpingitis the tubes are fibrous and thick-walled, and are often buried with the ovaries, uterus, bladder and broad ligaments in a solid fibrous mass, and the pelvic colon and pelvic coils of ileum also may be involved. In some cases, when the tubes are thickened and fleshy, numerous nodules may develop in the tubal wall and project both into the lumen and under the serous surface. Such a nodular thickening develops most frequently at the isthmus of the tube, i.e., where the tube joins the uterine cornu (*salpingitis isthmica nodosa*). Microscopically, the nodules contain numerous gland-like acini, are lined by mucous membrane, surrounded by hypertrophied bundles of muscle and fibrous tissue. It is presumed that in such cases portions of the mucous membrane have been forced by intra-tubal pressure into the muscle wall of the tube, and that the epithelium of the diverticula thus produced has proliferated as a response to the presence of a chronic infection.

Sometimes the lumen of the tube remains patent, but usually its two orifices become occluded, and it may then distend with watery fluid or with pus (*hydrosalpinx* and *pyosalpinx*).

*Hydrosalpinx* occurs when infection is of a mild degree. The tube is dilated by watery fluid derived from its lining cells and eventually it may attain considerable size and fill the greater part of the pelvis. The fimbriated orifice is occluded, partly by annular fibrosis, and partly by retraction of the fimbriae, and often the occlusion is so complete that the site of the orifice cannot be distinguished. The lateral end of the tube dilates to the greatest extent, and as dilatation is restrained by the peritoneal covering it gradually assumes a characteristic retort shape. The walls are sometimes thin and translucent and are readily torn.

*Pyosalpinx* results when the infection is somewhat more severe. The uterine ostium is occluded by oedema, and the abdominal ostium is closed either by indrawing of the fimbriae or by a kind of sucker

action, whereby the fimbriae adhere to adjacent structures. The tube becomes distended, but usually not to the same degree as in hydrosalpinx, for its walls are inflamed, thickened, and infiltrated with polymorphs, lymphocytes and plasma cells. Sometimes, especially in tuberculous infections, a pyosalpinx may attain great size. Often the surrounding tissues and coils of intestine are adherent. Not infrequently the abscess is not limited to the tube itself, but lies in a cavity walled in by adhesions between tubes, broad ligament and ovary, a *tubo-ovarian abscess*. The ovary itself may be infected, especially if a large Graafian follicle is present, and sometimes it is almost completely filled with pus.

Usually the pus is yellowish white and odourless, but it may be of a dirty colour and foul smelling. Often, despite this appearance, cultures yield no growth, for the causative organisms, gonococci and their associated non-haemolytic streptococci, tend to die out on prolonged sequestration. For this reason active surgical treatment is not usually required. In a few cases the abscess is infected secondarily by *Bacillus coli*, or other organisms.

**Tuberculous Salpingitis** Tuberculous salpingitis is not uncommon, but since the gross appearance often differs little from non-tuberculous salpingitis its specific character is not always obvious. The disease is invariably secondary to tuberculosis in other parts of the body, and is generally attributed to hæmatogenous infection. It is usually bilateral.

Tubercles develop in the mucous and submucous coats, which become infiltrated with lymphocytes and endothelial cells. Tubercles may develop also under the serous coat, and in this case the diagnosis on direct inspection is more easy. In many cases the tube is distended with caseous material so that it resembles a pyosalpinx. Adhesions surround the tube and bind it to adjacent viscera.

Tuberculous salpingitis is frequently associated with some degree of tuberculous peritonitis. In some of these cases it is possible that the tube is infected from the peritoneum, but more frequently the peritoneal lesions are secondary to tuberculosis of the tube. The practical importance of this is that removal of the diseased tube may promote recovery from the peritonitis.

### Tumours of the Uterine Tubes

Tumours of the uterine tubes are rare. The least uncommon are malignant adenoma and carcinoma. Papilloma, sarcoma, fibroma, teratoma, lymphangioma, and other forms have been described. Primary carcinoma occurs usually about the period of the menopause, and in 30% of cases is bilateral. It may be mistaken for chronic salpingitis, which it somewhat resembles. The tube is enlarged and thick, and may contain watery fluid or pus. Much of the lumen is occupied by a friable cauliflower-like growth which may be partly cystic. Usually the tumour is an adenocarcinoma. It is supposed to arise from the mucous membrane of the tubes, but an origin from Wolffian remnants in the parovarium has been suggested. In some cases there is evidence that the tumour arises on a basis of old inflammatory disease.

The uterine tubes are often involved in secondary carcinoma derived from the uterus, ovary, rectum, colon or stomach

## CYSTS AND TUMOURS OF THE OVARY

The ovary is a common site for cysts and cystic tumours. These vary greatly in nature and appearance. Many are of simple type, and result from distension of a Graafian follicle or corpus luteum, others have the characters of simple neoplasms, while yet others exhibit malignant properties. Solid tumours also occur in the ovary, but are less common. The cysts in most cases conform to regular types, but in certain proportion are of a mixed or atypical character, and defy exact classification. The following are the principal types —

### Simple Cysts

- (1) Follicular and luteal
- (2) Endometrial
- (3) Blood

### Solid and Cystic Tumours

- (1) Multilocular or compound cystadenoma (pseudomucinous cyst)
- (2) Papilliferous cystadenoma (papillary or serous cyst)
- (3) Teratoma (dermoid cyst)
- (4) Granulosa cell tumour
- (5) Arrhenoblastoma
- (6) Primary carcinoma
- (7) Secondary carcinoma
- (8) Connective tissue *e.g.* fibroma

### Follicular and Luteal Cysts

During the reproductive period of life a succession of changes occurs in the Graafian follicles, whereby they mature, discharge their ripe ova into the peritoneal cavity, and then develop into corpora lutea. It is certain that at least one ovum is set free during every menstrual cycle, and consequently the follicles which attain maturity between puberty and the menopause number several hundred. The normal ovary at birth, however, contains an immense number of immature follicles, probably in the neighbourhood of 30,000, and the vast majority of these gradually undergo atrophy or atresia. It is evident that in adult life the ovary will contain follicles in all stages of development, atresic follicles, immature and mature follicles, and corpora lutea, and any of these may undergo cystic change. It is generally believed that in adults the cysts arise principally in mature or almost mature follicles, but atresic follicles are also liable to cystic change. Cyst formation is usually attributed to chronic inflammation or congestion of the ovaries, but it must be admitted that there is not always evidence of this, and it seems likely that sometimes the origin is to be found in perversion of physiological processes in the follicle, rather than in any gross pathological factor.

*Follicular cysts* are most common during the reproductive period but they may occur in childhood or even in infancy. They are rare after the menopause. The cysts are usually multiple and bilateral, and in some cases both ovaries are almost completely involved. The cysts are generally small and rarely distend the ovary beyond the size of a golf ball.

The cysts are unilocular and contain watery fluid which occasionally is coloured by old or recent blood. The walls are smooth and fibrous, and the smaller cysts are sometimes lined by a single layer of columnar or cubical epithelium. Often the cyst wall contains lutein cells similar to those of the corpus luteum, but differing from them in being derived from the theca interna and not from the membrana granulosa of the follicle.

*Lutein cysts* are much less common than follicular cysts. They are usually single and may attain the size of a walnut, or even of a hen's egg. A characteristic feature is the presence of a thick fibrous wall of wavy contour and bright yellow colour. The wall contains numerous luteal cells, large rounded cells containing quantities of cholesterol and other lipoids to which the yellow colour is due. Sometimes a lining membrane of cubical cells is present. The content of the cyst may be clear watery fluid but it is often blood-stained.

Occasionally luteal cysts are multiple and bilateral (compound luteal cyst). These are usually related to pregnancy or to hydatid moles or choriocarcinoma. The cysts may attain the size of the foetal head. After parturition or after removal of the mole or carcinoma they may diminish in size (see p. 698).

### Endometrial Cysts (Chocolate Cysts)

Endometrial cysts of the ovary are most common between the ages of thirty and forty-five years and they are unknown before puberty and rare after the menopause. They are small cysts usually from 2 to 4 cm. in diameter and often both ovaries are affected.

The cysts are due to hæmorrhage from ectopic endometrial tissue (see p. 687) and on microscopic examination such tissue may be seen in small areas of the cyst wall. The hæmorrhage occurs at the menstrual



FIG. 311. Bilateral follicular ovarian cysts.  
(Department of Maternity and Gynaecology, University of Edinburgh.)

periods, for the ectopic endometrium undergoes the same cycle of functional activity as normal endometrium. The content of the cysts resembles menstrual blood. It remains fluid and acquires a tarry or chocolate colour.

An endometrial cyst, when small, lies under the surface of the ovary, but when distended by recurring bleeding it is very apt to perforate and to discharge its contents into the peritoneal cavity. The endometrial blood being irritant stimulates peritoneal adhesions, which generally are limited to the pelvis, but may sometimes implicate the intestines. In some cases the effused blood is not absorbed, but forms a fluid collection in the pelvis and becomes circumscribed by adhesions which bind together the ovary and the posterior surface of the uterus. The adhesions may be very dense and hard, and the condition may simulate a tubo ovarian abscess or a tumour. Continued activity of the aberrant endometrium may cause the fluid collection to increase in amount.

### Blood Cysts Haematomata

Hæmorrhage is most apt to occur in endometrial or in luteal cysts, but it is not infrequent in other types. In large cysts it is especially apt to arise when torsion or kinking of the pedicle leads to obstruction of the venous return. The ovary becomes tense with extravasated blood. The cyst may rupture, and a considerable amount of blood may then collect in the peritoneal cavity. In most cases, however, the blood clots and is ultimately absorbed. Occasionally infection of the clot leads to abscess formation.

### Multilocular Cystadenoma (Pseudomucinous Cyst)

This is the commonest of all ovarian tumours. It is a true tumour and results from proliferation of epithelial cells, which are probably derived from downgrowths from the germinal epithelium. The tumour undergoes cystic dilatation by the secretory products derived from its epithelial cells. As the tumour grows, its epithelium projects in various directions in a somewhat complicated manner, and in this way secondary foci develop either inside the principal cyst or in the substance of its wall.

Pseudomucinous cysts are usually unilateral, but in a small proportion they are bilateral. If untreated, they sometimes attain great size, and in pre operation days cysts of 50 lb or even 100 lb weight occurred. They rarely spread towards the broad ligament, and in the great majority of cases they become more and more pedunculated, and project upwards into the abdomen. The cysts are of rounded form and smooth surface, with undulations corresponding to the different loculi.

Microscopic examination shows that the cyst wall is composed of fibrous tissue lined by a layer of columnar epithelium. The epithelium consists of a single row of tall columnar cells, of remarkably uniform appearance. Each cell has a deeply placed nucleus and a peculiarly clear protoplasm. In places the epithelium is raised into papillary processes, but not so commonly as in the papillary type of cystadenoma.

The cysts contain glairy, mucoid material of aropy consistency.

Sometimes it is quite clear and almost colourless, but often it is turbid from debris and cholesterol crystals, and it may resemble pus. Often it



FIG. 312. Multilocular (pseudomucinous) cystadenoma of the ovary. A section of two portions of the cyst wall  $\times 275$ . The lining membrane is composed of tall columnar cells containing large globules of pseudomucin.

(Laboratory of Royal College of Physicians of Edinburgh.)

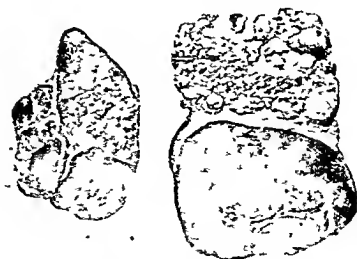


FIG. 313. Bilateral papillary cystadenomata of the ovaries.

(Department of Medicine and Gynaecology, University of Edinburgh.)

is tinged with altered blood pigment. The glairy material is pseudomucin, a substance that differs from mucin in its staining reactions and in the facility with which it may be precipitated by acetic acid.

The tumours usually follow a benign course, but there are intermediate forms which possess some of the characters of a papillary cyst.



FIG. 314. Papillary cystadenoma of the ovary.  $\times 275$ . The tumour is composed of columnar epithelial cells arranged in a papillary formation upon fine branching cores of connective tissue. The malignant character is indicated by the complex structure, by the nuclear hyperchromatism and by the presence of mitotic figures.

(Laboratory of Royal College of Physicians of Edinburgh)

adenoma, and these occasionally exhibit malignant properties. Pedunculation favours the occurrence of volvulus of the cyst. Occasionally a cyst ruptures and discharges mucoid material into the peritoneal cavity, leading to the condition of pseudomyxoma peritonei (see p. 548).

### Papillary Cystadenoma

Papillary cysts are much less common than the pseudomucinous cyst, but they are by no means rare. They are characterized by more vigorous growth on the part of the epithelial cells, which project either into the cysts or on their outer aspect, in the form of multiple warty or papillomatous excrescences. Both ovaries are usually affected. In each ovary there is generally one principal cyst, sometimes with a number of small subsidiary ones in its wall.

The cyst attains moderate dimensions, and rarely grows to such great size as a multilocular cystadenoma. It differs also in the character of the content, which is of watery consistency and contains albumin but no pseudomucin.

The most characteristic feature is the presence of papillary processes. Usually these are limited to one portion, and project internally into the cyst, but sometimes they cover the whole wall, and may grow to such an extent as to fill the greater part of the cyst. Not infrequently similar papillary processes grow also from the outer aspect of the cyst, and



project into the peritoneal cavity. This type is very apt to become malignant.

Microscopically, the cyst has a lining of low columnar or cubical epithelial cells, which are sometimes ciliated. The papillary processes which are covered with epithelium of a similar type, vary greatly in form. Some are of simple structure but others branch in complicated fashion and show evidence of proliferation.

Papillary cysts are on the borderline of malignancy and true cancerous change develops in a considerable proportion, probably about 20%. Malignancy is especially apt to take place when papillary growths project from the outer surface, but such projections are not a necessary prelude to malignancy. Frequently the cells are disseminated into the peritoneal cavity, and set up metastases either in the pelvis or throughout the abdomen. Such dissemination may occur even when the cyst shows no gross evidence of malignancy. Remarkably enough removal of the primary tumour may cause temporary retrogression or even disappearance of the metastases, though ultimately they almost always recur and prove fatal.

#### Teratoma (Dermoid Cyst)

Teratoma of the ovary is not uncommon, and is said to constitute about 10% of all ovarian tumours. It is generally described as a dermoid cyst but as it contains tissues derived from all the three embryonic layers it is rightly regarded as a teratoma. It is a benign tumour but in rare cases malignant change may supervene. The tumour grows slowly and rarely attains great size. In a small proportion of cases both ovaries are affected. The greater part of the tumour is cystic and contains fatty sebaceous material and often masses of hair and epithelial debris. The cyst is lined by stratified squamous epithelium in which hair follicles and sebaceous and sweat glands

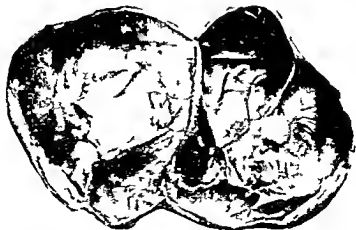


FIG. 315. Teratoma (dermoid cyst) of the ovary. A quantity of hair is seen growing from the wall and several teeth project inside the cyst.  
(Department of Obstetrics and Gynaecology, University of Edinburgh.)

may be recognized. At one side of the cyst there is usually a raised plaque and teeth may project from its surface. The wall deep to this plaque contains various tissues derived from mesoderm and entoderm. Cartilage, non striped muscle and glandular acini preponderate, and bone, thyroid tissue and even nerve cells may be present. Occasionally tissue resembling the chorionic epithelium is found.

It is obvious that such a teratoma arises from totipotent cells and there are two principal views in regard to its origin in the ovary. It has been suggested that it is derived from germ cells, ova that have undergone a kind of parthenogenetic development, for it is known that the ova of certain lower species may be stimulated to growth without fertilization by spermatoocytes. But such a theory takes no account of the occurrence of similar teratoma in the testis and there are other pertinent objections to its acceptance. The prevailing view is that the teratoma is derived from dislocated blastomeres which are known, in lower vertebrates at least, to be capable of forming a complete embryo.

### Granulosa-cell Tumour

This somewhat uncommon tumour occurs at any age, but especially in women who have passed the menopause. The tumour cells resemble the normal cells of the membrana granulosa of the Graafian follicle. The special interest of the tumour lies in the fact that it appears to produce an internal secretion which stimulates endometrial proliferation and leads to enlargement of the uterus and periodic hæmorrhages.

The tumour is generally unilateral, and usually of benign type. In a small proportion of cases, however, it is malignant. Generally, it is of moderate size, although there are examples recorded in which the tumour has attained the size of a man's head.

The tumour is encapsuled, with a thick fibrous sheath. It is partly solid, fleshy in appearance and somewhat vascular, partly occupied by cysts containing clear, straw coloured fluid.

Microscopically, the solid parts of the tumour consist of densely packed masses of polygonal cells, uniform in size, shape and staining qualities. These cells which sometimes show mitotic figures, resemble closely the cells of the granulosa layer of the Graafian follicle.

The cysts vary in appearance. The smaller ones are lined by a single layer of cuboid or flattened epithelial cells. The larger ones, on the other hand, show a characteristic structure somewhat resembling that of a normal follicle. The lining membrane consists of several layers of granulosa cells, closely packed polygonal cells with dark blue nuclei and scanty cytoplasm. The cells in the outermost part of this layer tend to be cuboidal in shape, and are supported on a basement membrane. In some cases outside the basement membrane there is a single row of clear or light staining cells resembling the theca interna of the follicle.

The origin of these tumours is not clearly understood. It has been supposed that they arise from adult granulosa cells of a mature follicle. That they generally occur in elderly women, and that they are sometimes found in the medullary part of the ovary, where mature follicles

do not occur, has led to the belief that they arise in embryonic rests present in the ovarian parenchyma

### Arrhenoblastoma

Thus rare tumour is interesting from the fact that it produces a hormone or group of hormones which alters the secondary sexual characters towards the masculine type. The tumour occurs at any age period between puberty and the menopause, grows rapidly and may attain very large size especially if cystic. It may be simple or malignant. Microscopically, it consists mainly of undifferentiated small round or spindle cells and may resemble a sarcoma. In some cases there are areas occupied by cells of epithelial appearance, arranged in cords or lining tubules somewhat resembling the testicular tubules.

One of the first results of the tumour is cessation of the menstrual periods. The condition may thus be mistaken for pregnancy, but may be distinguished by the fact that the Aschheim Zondek test is negative. Later the breasts atrophy, the hair of the head falls out or its growth ceases while there is an excessive development of hair on the lips and chin and on other parts of the body. The distribution of pubic hair assumes the masculine type and hypertrophy of the clitoris may develop. Operative removal of the tumour leads to restoration of the feminine characters. In some cases recurrence of the tumour has been followed by reappearance of the classical syndrome.

The origin of the tumour, and the nature of its hormones are not understood. It has been suggested that the tumour is derived from primitive undifferentiated germ cells in the hilum of the ovary, and that these cells acquire characters similar to the cells of Leydig, the interstitial cells of the testis.

### Primary Carcinoma of the Ovary

Primary carcinoma of the ovary is less common than secondary growths. It occurs in adults, frequently at a comparatively early period of life, and may affect nulliparæ or multiparæ. It usually arises in a pre-existing simple growth especially in a papillary cystadenoma, but it may arise *de novo* when it may be solid, or partly cystic from degenerative changes.

In many cases both ovaries are affected, but rarely to the same degree, and it is generally believed that the smaller tumour represents a secondary growth. The tumours rarely attain great size, and may be little larger than hen's eggs. In rare cases they grow rapidly and may assume large proportions. Sometimes they are of firm or even hard consistency, but often they are soft and almost brain like. Three types of carcinoma may be recognized, according to the microscopic appearances. (1) The common type occurring in a papillary cystadenoma has the structure of a malignant papilloma, and is composed of low columnar or cubical cells arranged in irregular papillary formation. (2) In other cases the structure is that of an adenocarcinoma, and the cells which show great diversity of form and staining reaction, are

arranged around irregular nuclei (3) Sometimes the tumour is composed of solid masses of cells, with no acinous arrangement—carcinoma simplex

Ovarian carcinoma very commonly disseminates through the peritoneal cavity, and secondary growths may be found in all parts, from the diaphragm to the pelvis, leading rapidly to hæmorrhagic ascites. In other cases it disseminates to lymph glands in the iliac and para aortic group, and to the uterine tubes and areolar tissue of the pelvis

### Secondary Carcinoma of the Ovary

The ovaries show a peculiar liability to attack by malignant cells derived from other sources. The stomach and colon are the common sites of the primary growths, but secondary ovarian deposits may follow cancer of the uterus, gall bladder or other abdominal organs and even cancer of distant regions, such as the breast. It is generally acknowledged that the avenue of implantation is through the peritoneal cavity, and it seems that malignant cells set free in the cavity reach the pelvic floor and the ovaries by transcælotomic gravitation.

Secondary growths often affect both ovaries. Usually the nodules are of small size, and are accompanied by metastases in other parts of the peritoneal cavity, but sometimes the ovarian deposits attain considerable size before others appear, may then be mistaken for primary tumour of the ovary, particularly if the primary tumour is a symptomless growth of the stomach or colon.

The microscopic appearance depends upon the character of the primary lesion, and this is usually an adenocarcinoma. In some cases the cells undergo "colloid" or mucoid change. They become distended by a clear substance resembling mucin, which displaces the nucleus to one side and gives a characteristic "signet ring" appearance (Krukenberg tumour).

### Uncommon Tumours of the Ovary

A *Fibroma* of the ovary is a rare tumour, and may occur at any age. It may be quite small or of great bulk, and is particularly prone to cystic degeneration.

An ovarian fibroma is of special interest in that on rare occasions it may be responsible for not only an ascitic effusion but also an intractable pleural effusion on one or both sides, usually more excessive on the right. The condition is known as Meig's disease, and was first described by Lawson Tait (1892). The curious phenomenon for which there is no satisfactory explanation, may simulate malignant disease. It is of particular interest in that the effusions disappear quickly and permanently after removal of the fibroma.

A fibromyoma resembling the uterine type, occurs occasionally, and is liable to the same forms of degeneration.

Endothelioma, melanoma, rhabdomyoma and choriocarcinoma are of rare occurrence.



FIG. 316 Ovarian metastasis (Krukenberg tumour) from a carcinoma of the colon. The tumour is composed of solid masses of epithelial cells which are distended to signet ring shape by intracellular globules of mucin.

(Laboratory of Royal College of Physicians of Edinburgh.)

*Sarcoma* of the ovary is rare. It occurs most often at puberty, but has been observed in childhood, and even in the foetus. It is sometimes bilateral. Spindle cell and round cell forms have been described. It is usually of great malignancy, and disseminates at an early stage.

### CYSTS IN THE BROAD LIGAMENT

The broad ligament contains a number of rudimentary structures derived from the Wolffian body and its duct. These structures are known collectively as the parovarium, and they are recognizable in the normal subject when the broad ligament is held up to the light. They consist of a main duct running medially in the base of the broad ligament and a number of short tubules communicating with it. The duct is the rudimentary Wolffian duct, or Gartner's duct. Laterally it ends blindly, medially it passes down parallel to the vaginal wall and it may open to the exterior in the neighbourhood of the hymen. The tributary tubules are collected in three groups. The ductuli transversi (Kobelt's tubules) lie at the lateral extremity of the broad ligament close to the ovarian fimbria, the tubules of the epoophoron lie in relation to the hilum of the ovary, and the tubules of the paroöphoron are situated more medially.

A cyst may arise from any part of the parovarium. The majority are small pea-like structures arising in Kobelt's tubules at the lateral end of the broad ligament and projecting freely into the peritoneal cavity. It is of little clinical importance. Less often, a parovarian cyst attains the size of a hen's egg, and even greater. It is a smooth,

translucent, unilocular structure, which can be readily separated from the peritoneum and enucleated. It consists of a fibrous wall lined by a single row of low columnar ciliated cells, and contains clear, watery fluid of low specific gravity.

Occasionally a cyst in the broad ligament attains great size so that it fills the pelvis and extends upwards into the abdomen. Recent

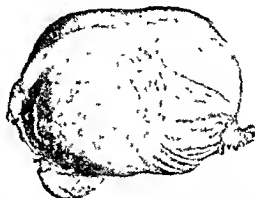


FIG. 317. Cyst of the broad ligament. The Fallopian tube is displaced by the cyst and is incorporated in its wall. The ovary lies below at the left side.

(Department of Medicine and Gynaecology, University of Edinburgh.)

researches suggest that the majority of these cysts arise not at the parovarium but in the displaced ovarian or mesonephric tissues lying in the ovarian fimbria. The uterine tube and fimbria are stretched out over the surface and the ovary is incorporated in the wall, so that it is only distinguished with difficulty. Such a cyst usually resembles true parovarian cysts in structure, but sometimes in place of clear fluid it contains pseudomucin. Occasionally intracystic epithelial projections occur, as in papillary cystadenoma.

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